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REAPPRAISAL OF SURGICAL TREATMENT OF MAMMARY CARCINOMA

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The inevitable handling of soft tissues during mastectomy for mammary carcinoma increases the danger that tumor cells may be carried to nearby lymph nodes. Metastases laterally toward the axillary lymph nodes are visible and accessible and have received much attention. Metastases medially toward the supraclavicular and internal mammary nodes have not received sufficient attention, although they constitute the greater danger. The danger can be reduced by the type of operation here described. In it, the first incision is planned to block lymphatic and venous draining in the medial direction before beginning the extensive manipulations involved in mobilizing the primary breast tumor and dissecting the axillary structures.

IT IS the purpose of this study to reappraise the traditional procedure of radical mastectomy and to indicate the advantages of interruption of the pathways of lymphatic spread to the medial chain of lymph glands, in the initial stages of the operation, with a minimal amount of operative manipulation. The preferred therapy for breast carcinoma since 1894 has consisted chiefly of radical mastectomy performed according to the technique developed by Halsted[1] and Meyer.[2] Well-performed radical mastectomy can effect a cure of mammary carcinoma if no viable tumor remains in the patient at the completion of the operation. In view of the extensive dissection and handling of soft tissues in the performance of mastectomy, one should always be concerned with the threat of embolization of tumor cells produced by the manipulations in the course of the operation. Although lymphatic spread to the axillary glands is the most common route, the tumor is usually resectable in the axillary glands.

It is, however, the lymphatic spread to the supraclavicular and internal mammary chain of lymph nodes on the medial side of the breast that renders the carcinoma incapable of cure. One can only conjecture how frequently the embolic spread of carcinoma cells to these medial lymph glands occurs during the manipulations and dissections of radical mastectomy. Yet in spite of this knowledge the traditional radical mastectomy consists of a dissection proceeding from a lateral to a medial direction, with all the concomitant massage and manipulation which tend to encourage the lymphatic embolization of tumor cells to the medial chain of lymph nodes out of the range of resection by the commonly performed radical mastectomy. It is only in the final stages of this extensive dissection that the lymphatic routes to these medial lymph nodes are finally interrupted. No intermediate lymph glands exist on the medial side of the breast

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within the resected portion of tissue to act as filter traps for the free-floating tumor cells in the lymphatics during the course of the resection.

The presence of clusters of carcinoma cells in lymphatic vessels and also in the peripheral sinuses of lymph glands in the surgical and autopsy specimens of mammary carcinoma evidence the active lymphatic embolic spread. It seems a simple corollary that the more extensive the manipulation and massage of cancerous tissues the greater will be the opportunity for embolic metastases. The importance of gentleness in handling malignant tissues has been stressed by Halsted, Meyer, and many investigators since their time. In 1913 Tyzzer[3] demonstrated that gentle massage of a transplanted carcinoma in a mouse greatly increased the number of metastases observed in the lung. Further experimental evidence was provided by Knox,[4] who demonstrated that gentle massage of breast tumors in the mouse increased the number of tumor emboli, which can produce metastatic tumors. The recent work of Roberts and co-workers[5] shows that there is an increase in the number of cancer cells in the circulating blood during the manipulations of resection of the tumor in human patients.

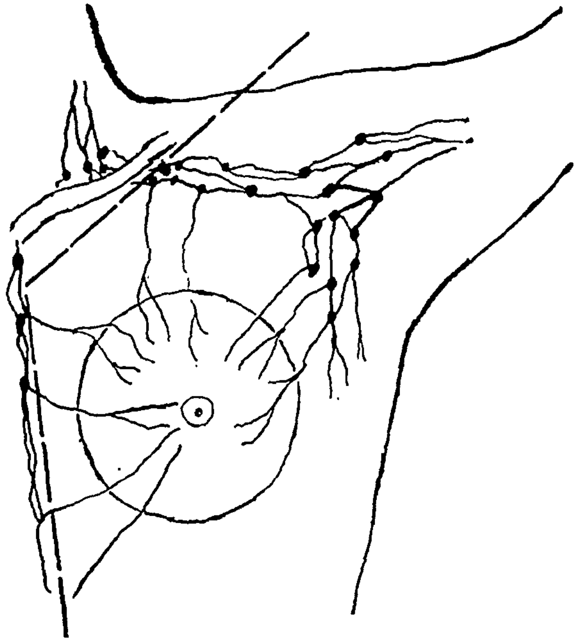

Fig. 1.—Diagrammatic illustration of lymphatic system involved in mammary carcinoma. *Broken line indicates sites of surgical interruption of the lymphatic channels as they course medially from breast and axilla.*

As a practical therapeutic approach one could, as a matter of thought, consider the primary carcinoma in the breast and the axillary gland metastases to be a functioning malignant unit, since routine surgical pathological studies indicate that the axillary glands are involved in one-half to two-thirds of cases. Both of these areas tend to spread through the lymphatic channels in a medial direction to the supraclavicular and internal mammary lymph glands.

Lateral Dissection Versus Medial Dissection as First Procedure

In radical mastectomy the lateral mobilization, consisting of the elevation of the lateral skin flap, the axillary dissection, and the mobilization of the breast from the lateral chest wall, is accompanied by much more manipulation and massage of cancer-bearing tissues than is the medial dissection, which consists of elevation of the medial skin flap, dissection of the breast and pectoral muscle origins from the thoracic wall, and division of lymphatics coursing medially beneath the clavicle. If the lateral dissection, as described above, is performed before the medial dissection in radical mastectomy, the lymphatic drainage to the medial chain of lymph glands in the supraclavicular and internal mammary chain is left intact during the extensive manipulation and massage of the dissection. The extensive lateral dissection tends to create a situation which encourages, by mechanical manipulation, the embolization ahead of the dissection through lymphatic channels which have not yet been interrupted and which do not contain lymph glands to act as filter traps.

Why is the lateral mobilization performed first? There are several significant reasons: 1. It is traditional as described by the original techniques of Halsted and Meyer and by the breast surgeons who have had extensive experience since that time. 2. The more technical portion of the dissection, mobilization of the breast from the lateral chest wall and the delicate axillary dissection, is completed in the early stages of the operation. It is a natural human tendency to do the more technical procedures early. 3. It is easier to maintain hemostasis of the perforating arteries and veins as they come through the chest wall from the internal mammary vessels after complete mobilization of the breast and pectoral muscle than prior to the mobilization.

Why should the surgical dissection and mobilization of the medial side be performed first? 1. First and foremost this approach interrupts the lymphatic channels from the primary tumor in the breast and the axillary lymphatic metastases, if they are present, to the supraclavicular and internal mammary nodes and to the lymphatics of the round ligament before the hydraulic massage of the extensive axillary and lateral breast mobilization. The lymphatic drainage of the breast is diagrammatically illustrated in figure 1, with the interrupted line representing the surgical intersection of the medial lymph channels. 2. A breast of moderate or large size is naturally inclined over the lateral aspect of the chest when the patient is in the supine position. This makes the elevation af the medial skin flap and the medial mobilization of the dissection more anatomic and necessitates less massage than does lateral mobilization and dissection. It utilizes the force of gravity, inclining the breast toward the lateral side of the chest for retraction, and it requires less manipulation to produce retraction. 3. There exist no intermediate lymph glands to act as filter traps between the medial chain of glands, consisting of the supraclavicular and internal mammary chain on one hand and the mammary gland and axilla on the other. 4. As a basic principle of cancer surgery it is advisable to attempt to interrupt the most distant route of spread that is feasible before the mobilization of the involved cancerous tissue. By analogy, in cancer of the rectum and rectosigmoid colon the highest point of lymphatic spread along the inferior mesenteric circulation is interrupted prior to mobilization and manipulation of the primary growth. Similarly, if one considers the primary breast tumor and axillary glands as a functioning malignant unit, since they are so commonly involved together, then one should logically first interrupt the most distally acceptable route of spread in the initial stages of the dissection before mobilizing the tissues involved by the malignancy. 5. The medial dissection simultaneously interrupts many of the venous routes of tumor spread as well as the lymphatic channels.

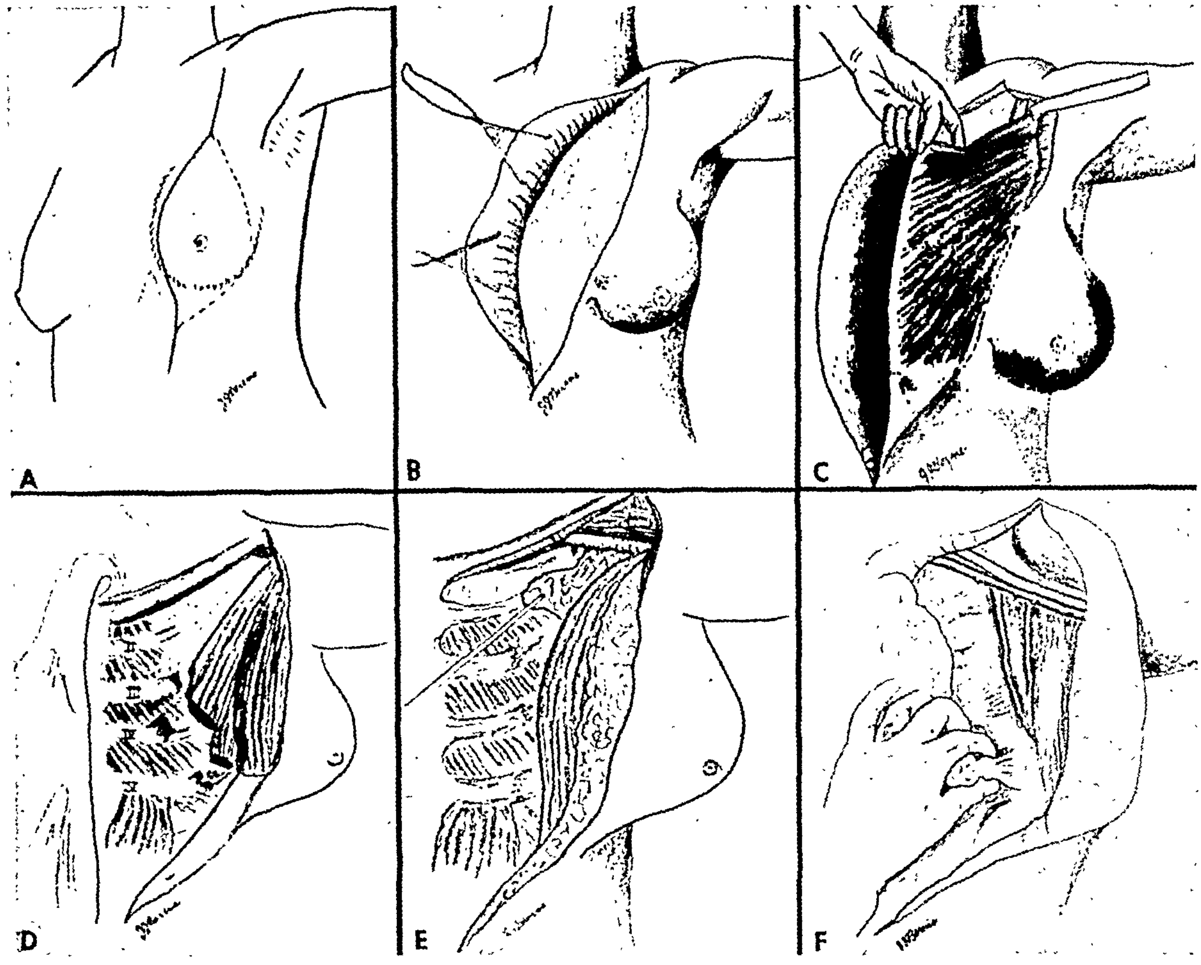

Fig. 2.—*A*, outlines of skin incisions for radical mastectomy. Medial skin incision is made along continuous line. Dotted line is for lateral skin incision, not made until all medial routes of spread are interrupted. *B*, medial skin flap is elevated with help of special skin flap hooks. Note that gravity force retracts breast laterally during dissection to reduce need for manual traction on tumor in breast. *C*, elevation of pectoralis major muscle, allowing division at its origin. *D*, elevation of pectoralis minor muscle, allowing division at its origin. *E*, deep axillary fascia is opened in subclavicular area to remove subclavicular lymph nodes and divide lymphatic channels before they course medially beneath clavicle to supraclavicular lymph glands and systemic venous system. Exposed tissues are then covered with moist compresses before lateral skin incision is made. *F*, radical mastectomy is completed by severing remaining structures from chest wall.

Preferred Operative Technique for Radical Mastectomy

Surgical management starts at the time of the physical examination of the breast for malignancy. Gentleness in the course of the physical examination of the breast tumor and axillary nodes is of obvious importance in reducing the amount of mechanical massage and manipulation to the suspected carcinoma. It is also worthwhile to advise the patient not to examine her breast any further between the time of the examination and the time she enters the hospital for definitive treatment. Many patients are prone to continue repeated self-examinations, since their attention is so strongly focused on the breast pathology.

In the operating room the surgical preparation of the field of operation should be either performed or supervised by the operating surgeon. Frequently the breast and the axillary area are prepared with such vigor in the mechanical cleansing of the skin that the massage is conducive to embolization of tumor cells. The cleansing and skin preparation should be adequate but gentle.

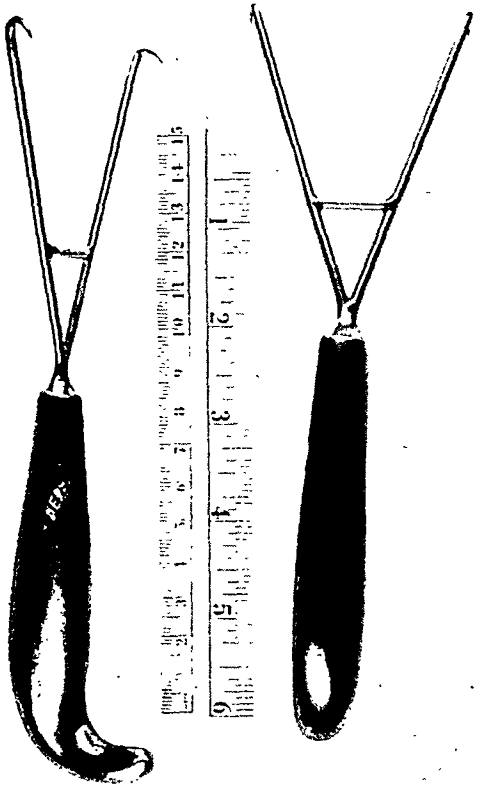

Fig. 3.—Mastectomy skin flap retractor.

Lines are then marked on the skin for vertical incision with the back of the point of the knife blade (fig. 2*A*). I use the vertical type of incision, encircling most of the mammary gland, going widely around the area of the tumor, and extending in a cephalad direction over the clavicle along the strap line.

The medial skin incision (fig. 2*B*) is then made with the operating table tilted laterally toward the side of the affected breast to aid in retraction by the force of gravity acting on the breast to displace it in a lateral direction. An adequately thin skin flap is prepared, extending the dissection to the midline over the sternum and to the clavicle.

Starting at the cephalad portion of the field the pectoralis major muscle is divided near its origin from the clavicle (fig. 2*C*). With the finger as the retractor the pectoralis major is elevated from the thoracic wall and dissected at its origin from the sternum and ribs. The perforating vessels from the internal mammary circulation are isolated, clamped, and divided as they are approached. The dissection is carried in a caudad direction and includes a portion of the anterior rectus sheath. The origin of the pectoralis minor muscle is similarly dissected from the chest wall (fig. 2*D*).

The deep pectoral fascia is then entered in the subclavicular area. Dissection is continued along the axillary vein to the point where it emerges beneath the subclavius muscle (fig. 2*E*). The subclavicular nodes, which usually number two to five in this area, are dissected out in continuity with the specimen. It is advisable to leave a long silk suture as an identification mark for the pathologist in the area of the subclavicular glands. The pectoralis minor muscle insertion is mobilized with finger dissection, clamped, divided, and ligated. Further dissection is carried medially from this area, isolating, clamping, and dividing the branches of the thoracoacromial vessels.

At this stage of the dissection the accessible medial lymphatic and venous routes of spread have been interrupted before the lateral skin or deep mobilization of the dissection has been started. It is this latter form of dissection which is accompanied by stronger traction and manipulation of the breast and axilla, which is conducive to embolization of tumor cells. The exposed area is then packed with moist compresses to protect the tissues from drying and to attempt to collect any carcinoma cells which pass through the severed ends of the lymphatic and venous channels during the remainder of the dissection. Whenever these gauze packs are disturbed, it is advisable to replace them with fresh ones rather than rearrange them.

The operating table is then tilted laterally toward the side of the uninvolved breast to allow the involved breast to be disposed in a medial position and thus permit the force of gravity to aid in medial retraction. The skin incision for the lateral flap is then made and the lateral skin flap is elevated. As the anterior border of the latissimus dorsi muscle is approached the thickness of the skin flap is increased. The dissection is continued laterally beyond the border of the latissimus dorsi muscle as an aid in mobilization of skin to facilitate closure of the skin flaps at the completion of the operation. Moist compresses are placed against the exposed tissues.

The pectoralis major muscle is then severed at its tendinous insertion into the humerus. Usually no bleeding follows the division of the insertion of the major muscle, if this is done at its tendinous portion. A small bundle of clavicular fibers of the pectoralis major frequently are left intact. The axillary vein is isolated by sharp dissection, and all branches are clamped and divided, since they course into the area of the resected specimen. The medial border of the latissimus dorsi muscle is mobilized and the axilla is entered from the inferior aspect. By sharp dissection all lymphatic and fatty tissues are excised in continuity with the breast. The thoracodorsal and long thoracic nerves as well as the subscapular vessels are preserved, if they are not involved in the neoplasm. The resection is completed by dissecting the remaining tissues from the thoracic wall (fig. 2*F*). The operative wound is thoroughly irrigated with saline solution, strict hemostasis is secured, rubber drains or suction catheters are inserted, and the skin flaps are reconstructed.

The dissection of large skin flaps, as in simple radical mastectomy procedures, is greatly facilitated by use of a retractor (fig. 3) which fulfills several requisites. These include (1) elevation of the skin flaps over a broad surface area to allow good exposure for the dissection, (2) minimal trauma to the tissues, (3) secure contact between the retractor and the skin flaps, and (4) adequate vertical tension of the skin to facilitate sharp dissection of thin skin flaps. The retractor shown in figure 3 contains two sharp hooks located 2½ in. apart. The use of two retractors placed several inches apart on the same skin flap greatly facilitates the dissection of the cutaneous flaps during mastectomy.

Summary and Conclusions

There is need for a modification of the surgical treatment of mammary carcinoma from the standpoint of interrupting the routes of embolic tumor spread in the initial stages of the treatment. I feel strongly that in some instances viable tumor cells spread beyond the confines of the resected tissues during the course of the traditional radical mastectomy as a result of the massage and manipulations engendered by the lateral and axillary dissections, and I have outlined an operative procedure which interrupts the accessible routes of medial embolization in the early stages of the operation, before any manipulation of the primary breast tumor or the main axillary dissection is performed.

550 W. Thomas Rd.

The mastectomy skin flap retractor is made by V. Mueller & Co., Chicago.

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PREOPERATIVE PSYCHIATRIC CONSULTATION

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Preoperative psychiatric consultation can help not only in cases in which operation may be contraindicated from the psychiatric viewpoint but also in cases in which operation will prove to be helpful. By critically reviewing the diagnosis of psychoneurosis, the psychiatrist has been responsible for operations that have proved lifesaving. Also, through careful evaluation, the psychiatrist can determine when an indicated surgical procedure is not likely to result in relapse into an earlier psychiatric condition. Five case reports illustrate these various possibilities.

With the growing acceptance and application of psychiatric principles, there has been an increasing demand for psychiatric consultations with medical and surgical patients. In the past, psychiatric consultations with surgical patients almost invariably followed operation. Cases were included in which the patient had become dependent on narcotics or in which surgical exploration had failed to reveal any pathological condition and the surgeon had concluded that the symptoms were psychogenic. Another equally troublesome and puzzling group of cases was that in which surgical removal of the pathological condition failed to remove the symptoms and, in fact, sometimes made the patient worse.

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Many surgeons in recent years have become more wary regarding elective operations and frequently request psychiatric consultation preoperatively. In the case of emergency operations, or nonelective operations such as operations for cancer, the psychiatrist's decision is easy. He indicates that, although postoperative psychiatric complications may well occur, there is no alternative but to operate and to handle the complications later. Even in these cases, however, it is desirable for the psychiatrist to have some knowledge of, and relationship with, the patient before operation.

Psychiatric Contraindications to Surgical Intervention

Many surgeons have intuitively recognized a poor surgical risk from the psychiatric viewpoint or have learned from sad experience the type of patient who should not be offered elective operation. These patients, however, are more easily recognized by the psychiatrist, and he has a better understanding of the basic dynamics involved. Thus, the psychiatrist can help the surgeon to formulate a program of treatment that is more conservative than a surgical approach. In fact, in many of these cases the preoperative psychiatric consultation results in psychotherapy rather than in surgical treatment. Two well-known categories include the paranoid patient, usually male, and the hysterical female.

It is generally accepted that elective operations, particularly in the genital region, are to be avoided in paranoid males. The symbolic significance and the distorted interpretations put on such operations by these patients often have led to tragic circumstances. Also well known are the female patients with basically hysterical masochistic personalities and great masculine protest who never seem to rest until all vestiges of their female anatomy are removed. These are the women with incapacitating abdominal and perineal pain who have undergone long series of operations in which their reproductive tracts have been removed piecemeal until they are eventually rendered neutral. However, the pain and animosity toward the surgeon remain unaltered. It is a truism in these cases that surgical procedures fail to relieve the patient of a disabling symptom because an attempt has been made to remove surgically the somatic expression of an emotional illness. Such attempts all too often merely lead to repetition of the symptoms.[1]

Other guides, which perhaps are known but which are not well defined, can help the psychiatrist in aiding the surgeon. The absence of organic findings is not a sufficient reason for establishing a psychiatric or "functional" diagnosis. A common error of our nonpsychiatric colleagues is to label a symptom as psychogenic because examinations did not reveal organic findings. This is a negative approach. Positive psychiatric findings must be obtained to support a psychiatric diagnosis.[2]

Significant Factors in Psychiatric History

If psychiatric opinion is to be based on positive psychiatric evidence rather than on intuition or on absence of organic findings, it is necessary to stress the importance of a carefully taken psychiatric history. Certain areas of the history are of greater significance than others in helping the psychiatrist to formulate his opinion. Several suggestions are presented and will be illustrated later in reports of cases.

Genetic material may reveal a significant person in the patient's environment who had a similar or somewhat similar illness. In these cases it is helpful to know the patient's reaction to that person and to the illness. Many times a hostile identification is made by the patient with this significant person resulting in an almost learned method of reacting to stress by means of illness.

Significant events surrounding the onset or the recurrences of the symptom may be pertinent. Some of the commoner events are death or separation from a parent, spouse, or lover, difficulties in relations with an employer or some parental figure, or threat of illness. Consequently, when taking a detailed history it is necessary to identify not only the members of the patient's immediate family but also the important personal contacts in his business, social, and sexual life.[3]

The symbolic significance of the patient's symptom or involved organ to him is a factor. There are certain portions of the body which are commonly endowed with a great amount of symbolic significance. Already mentioned are the genitalia and the reproductive system. Another common region is the back, and pain in the back is notoriously hard to evaluate. Admittedly, the symbolic significance of a pain or symptom rarely becomes apparent in an initial diagnostic interview, but some clue is frequently obtained when the data are correlated with other material.

Important also are the history of previous illness and surgical experience and the patient's reactions and recovery from them. It is safe to assume that a patient who has undergone three operations on the back for the relief of pain and has had poor results most likely will not benefit from a fourth operation. The tendency to regress seriously and become dependent on narcotics after previous operations should be considered carefully.

The manner in which the patient discusses his symptom is also quite revealing. The bland indifference of the conversion hysteria patient is well known, as is the highly dramatic patient whose symptoms are far out of proportion to the findings. A sensitive, well-trained psychiatrist will note certain more subtle factors, for example, the symptom is often precipitated or aggravated by discussion of topics emotionally distressing to the patient.

The element of secondary gain should be considered. Although this may be unconscious as far as the patient is concerned, it is a real factor. The patient is in need of the symptom to control his environment, as in the case of a woman whose symptom is used as a club to keep an errant husband in line, or, in the frigid woman, as an excuse to avoid sexual relations.

The following condensed reports of two cases will serve to demonstrate some of these points.

Report of Cases

Case 1.—A 38-year-old woman was seen at the Mayo Clinic in 1955, at which time she complained bitterly of incapacitating pain in the back and in the sacral region extending down both legs. She was unable to sit and she walked with cautious mincing steps. An extensive examination was done, and nothing of a positive nature was discovered. The neurologist felt that her disability was far out of proportion to her symptoms and asked for a psychiatric opinion for diagnostic purposes.

Her father was an alcoholic who was abusive to the patient and her mother. The mother was a long-suffering masochistic woman who frequently "took to bed" with pains in the chest when the patient's father was particularly brutal. The patient married a rather passive man, and both were disappointed that she could not have children after removal of both tubes and one ovary, which were said to be diseased. The patient "did not get back on her feet" for one year after this operation, which was done shortly after her marriage. She had always been frigid and had avoided intercourse.

The onset of the pain in her back came on within a short time after she discovered that her husband was having an affair. She acknowledged that since the onset of the pain her husband had been solicitous and remorseful. Also, she had successfully avoided intercourse since the onset of her symptoms. The patient was lying down during the entire interview; she was extremely dramatic and smiled frequently while telling of current excruciating pain.

This history was shared with the orthopedist and neurosurgeon with the strong recommendation that surgical procedures be avoided in that there was overwhelming psychiatric evidence that the patient's problem was an emotional one. Psychotherapy was advised, but the patient refused.

She returned in 1958 with exactly the same complaints and was even more disabled. She had undergone three surgical procedures elsewhere in the interim with no relief and with great venom toward the "incompetent surgeons who operated on me." A conservative program of psychotherapy and physical therapy was outlined for her.

Case 2.—A 54-year-old woman was injured in an automobile accident in 1949 and had persistent pain in her neck and in the lower portion of her back. She complained also of numbness of the right arm. She had spent all but one hour of each day in bed for the previous three years because of the pain. She had undergone two operations elsewhere for removal of a protruded intervertebral disk, and on the second occasion the fourth and fifth lumbar vertebrae were fused. Her recovery from the operations was slow, and she had the problem of addiction to meperidine (Demerol) after the second operation. The examinations revealed some positive neurological findings and narrowed vertebral interspaces in the low cervical and lumbar portions of the spinal column. Operation was considered but was abandoned in favor of a conservative program after completion of the psychiatric study, which revealed a masochistic personality with much secondary gain and control of her environment by means of her symptoms. The lack of success of the previous operations and the psychiatric complications after the second influenced the decision to avoid operation despite the strong evidence of the presence of a pathological condition.

Comment.—The patient in the first case demonstrated hostility and a masochistic attitude toward men, the identification with the mother who had a need for illness, and the onset of the patient's symptoms after discovery of her husband's infidelity. Both patients showed evidence of secondary gain and the control of the environment by means of illness and pain. Both patients also showed poor responses to and results from earlier operations elsewhere. Actual dependence on narcotics was evident in case 2. Both patients exhibited dramatic attitudes with disability being far out of proportion to the findings.

Fortunately, operation was avoided in these two cases, which are prototypes of many similar cases. The existing symptoms would have been further fixed and additional disability would have followed if an operation had been performed.

Negative Results of Psychiatric Examination as Guide to Surgeon

Heretofore I have discussed recognition of patients in whom surgical intervention is contraindicated from the psychiatric standpoint. Of equal help to the surgeon are those cases in which the psychiatric interview used as a diagnostic tool can predict when surgical procedures will be helpful.

Case 3.—A 42-year-old man came to the clinic with a history of recurrent severe pain in the right upper quadrant extending around the right costal margin to the lower edge of the right scapula. Nausea or vomiting was not associated with the pain, and relief was obtained only with narcotics. The pain was sufficiently frequent and disabling to prompt the patient to request exploratory laparotomy. The results of exhaustive tests and examinations were negative, as they had been elsewhere. A psychiatric opinion was requested by the surgeon. The psychiatric examination did not reveal significant psychopathological factors. The patient had an excellent work record, and family and marital adjustments were normal. No precipitating event was found from an emotional standpoint, no secondary gain was apparent, and no typical somatic expression of an emotional conflict was evident in the manner in which the patient discussed his symptoms. These data were recorded on the patient's chart, and the surgeon was notified that the patient's pain could not be ascribed to psychiatric causes and that laparotomy was justified.

At operation a subacute perforating postbulbar ulcer was found, and gastrectomy was performed. The patient made an excellent recovery, returned to work, and has been asymptomatic.

Comment.—It should be emphasized that a history that is void of significant psychopathological evidence as in case 3 is quite different from the bland "everything and everyone is perfect" type of history characteristic of the hysterical personality.

Carcinoma of the pancreas has frequently been diagnosed as a psychogenic illness owing to the unusual nature and pattern of the pain. Here again the psychiatric interview has been helpful in discounting the diagnosis of psychoneurosis, and in a few instances the psychiatrist has actually made the diagnosis of carcinoma of the pancreas.

Psychiatric Indications for Surgical Intervention

Not so well known are cases in which operation will be beneficial to the psychiatric disorder as well as to the organic pathological state. This is particularly true in the depressions encountered among patients in the older age group. It is almost as if the discomfort of the operation is sufficient to assuage the patient's guilt which has been feeding the depression.

CASE 4.—A 64-year-old man was admitted to the psychiatric unit because of depression of several months' duration. The depression had become progressively worse with suicidal thoughts. In addition, the patient gave a history of increasing urinary difficulty indicative of prostatic obstruction. Transurethral prostatectomy was indicated, but the consulting urologist was reluctant to operate in view of the patient's depression. I indicated a preference for having the operation performed before electroshock therapy was undertaken in the hope that the depression would be lessened. Prostatectomy was performed, and the result was excellent. The patient was relieved of depression to the extent that electroshock therapy was avoided and he returned to his job.

Comment.—Obviously surgery cannot be endorsed as psychiatric therapy, but in a few carefully selected cases it can be helpful. Also in this category are those cases in which the surgeon feels an operation is indicated but is reluctant to operate due to a previous or current serious psychiatric diagnosis. Many physicians are of the opinion that psychiatric patients generally will have a difficult postoperative course because of the emotional decompensation as a result of operation. By and large, the reverse is true. Patients with diagnoses of schizophrenia and depression, for example, are not as brittle as is often thought; in fact, they seem to meet the stress of surgical procedures with surprisingly good ego strength.

CASE 5.—A 32-year-old housewife had been hospitalized on several occasions with a diagnosis of schizophrenia. This diagnosis was made at the age of 24 years, and since that time the patient had been able to function at home relatively well between relapses. She had three children and had had postpartum schizophrenic relapses after the first two deliveries. She was seen psychiatrically during the third pregnancy as she feared a relapse. However, she got along unusually well during her pregnancy and the postpartum period except for some mild gnawing abdominal pain which she ascribed to her pregnancy. When the pain persisted after delivery, a roentgenogram of the stomach was made, which revealed a huge prepyloric gastric ulcer on the posterior wall of the stomach. In view of the psychiatric history, the internist and surgeon felt that nonsurgical management would be best, although a surgical procedure would be the treatment of choice. The psychiatric opinion was to the effect that the patient would probably withstand operation satisfactorily, especially in view of her ability to carry through her pregnancy and delivery without decompensating. Consequently an operation was performed; carcinoma of the stomach was discovered, and the lesion was removed. The patient withstood the operation well and also accepted the diagnosis in a realistic manner. She was able to function in a most satisfactory fashion postoperatively as determined by psychiatric follow-up.

Comment.—Psychiatrists are aware of numerous instances of remissions from schizophrenia that have occurred after the stress of serious surgical measures. The general tendency to avoid operation when there has been a history of psychiatric decompensations is not warranted.

Summary

Psychiatrists are in a unique position to assist the surgeon in cases of elective operation by properly evaluating the patient's symptoms by means of a careful psychiatric history. There are guideposts for the use of accepted principles to replace intuition. Psychiatric consultation is valuable not only in cases in which operation is contraindicated from the psychiatric viewpoint but also in those cases in which operation will prove to be helpful.

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CINEMATOGRAPHY OF HUMAN RETINAL VESSELS

A PRACTICAL CLINICAL AND RESEARCH TECHNIQUE

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In recent years, functional changes in the retinal vessels and other structures of the fundus have become increasingly important to clinicians and others. Changes not readily discernible with ophthalmoscopy or serial still photography can be demonstrated by a practical technique of cinematography designed and in use at the University of Oregon Medical School. With a special camera, variations in amplitude, character, and rhythm of pulsation of the retinal arterial system can be detected for research and teaching purposes, and to aid in differential diagnosis, or to permit early evaluation of therapy. The camera contains three basic units: a mounted +20 D. condensing lens, a light source with means of changing magnification, and the camera body containing film and a continuous focusing device.

Ophthalmoscopy has become a part of the routine general physical examination; however, fundus studies with the hand ophthalmoscope primarily have been directed toward the recognition and evaluation of morphologic changes in the retinal vessels and other structures of the fundus. These changes generally can be recorded satisfactorily with commercially produced cameras which take single-frame pictures. In contrast, functional changes such as in the character and amplitude of pulsation of the retinal vessels or in the movement of blood through them have received relatively little attention. In recent years these functional changes have become increasingly important to clinicians and investigators in several fields of medicine, but there has not been a satisfactory way to record these alterations for research, teaching, or records of individual patients. For example, in systemic vascular disease such as atherosclerosis, early clinical manifestations are difficult to detect; therefore, criteria for evaluation of therapy early in the course of the process generally are inadequate. An effort has been made to recognize changes in elasticity or reactivity of the retinal vessels as possible early manifestations of systemic vascular disease. In hypertensive disease, Sieker and Hickam [1] have evaluated this factor by studying the constriction and dilatation of the retinal arterial tree while the patient breathed oxygen. They have demonstrated these changes by still photographs of the fundus, but in our experience alterations in caliber and amplitude of pulsation are more readily discernible in cinematography.

Another indication for study of the retinal vessels, of particular importance to neurologists and neurosurgeons, has been occlusive disease involving the carotid system. In occlusion of the internal carotid artery there is a decreased amplitude of pulsation of the retinal arterial system. This sometimes can be measured by ophthalmodynamometry. Unilateral alterations in the amplitude of pulsation of the retinal vessels also occur in carotid-cavernous sinus communication and in some basilar aneurysms. Alteration in amplitude of the retinal venous pulse is of value in the differential diagnosis of papilledema. In true papilledema, in contrast to pseudo-papilledema, there is absence or decrease in venous pulsation at the optic disk. From the viewpoint of the ophthalmologist concerned with ocular disease, the relationship of the retinal and choroidal arterial circulation to the intraocular pressure and to changes which take place in inflammatory disease needs to be more thoroughly investigated.

From examples cited above it is evident that a practical technique of cinematography to record the pulsations in the retinal circulation would be valuable for recording changes in the individual patients and for research purposes. From the viewpoint of teaching ophthalmoscopy to undergraduates and physicians, fundus cinematography has proved to be an important adjunct at the University of Oregon Medical School.

The major reason for the limited use of cinematography since Pavía [2] called attention to it in 1952 has been the technical difficulty involved in taking these pictures. The tolerance of the human eye to light is limited. Furthermore, high concentrations of visible light are capable of producing irreversible damage to the retina, e. g., eclipse blindness.

Several approaches have been made to this problem. In experimental animals it has been possible to remove the anterior segment of the eye and replace it with a glass surface. This technique was used by Ashton [3] in recording the changes induced in the retinal vessels in the kitten eye by systemic administration of oxygen. Another technique which we have used until recent years has been to add a movie film carrier to the Nordenson type of fundus camera. This system does not permit continuous

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From the Department of Ophthalmology, University of Oregon Medical School.

focusing and is too inefficient to obtain consistently good films even with high-speed film. Still another technique has been to use a television camera and to record film from the face of the television tube.[4] It seemed to us that if cinematography were to be made useful as a clinical and research tool, it would be necessary to design a camera which could be produced at a reasonable cost and which could be used with a majority of patients. Such a camera has been designed at the University of Oregon Medical School and has been used since 1957.

The camera contains three basic units. The first unit consists of a mounted +20 D. condensing lens as is used in indirect ophthalmoscopy. The second unit contains a light source and a means of changing magnification. It consists of the body of a Zeiss dissecting microscope. This particular microscope provides a range of four magnifications. Also, it contains a built-in filter system and an efficient source of para-axial illumination. The light is directed through the condensing lens and pupil at a slightly oblique angle. The third unit consists of a camera body which carries film and contains a continuous focusing device. For continuous focusing, it is almost essential to have a through-the-lens system such as is provided by the 16-mm. Arriflex camera. No light is lost by this system and it permits the operator to shift the field, to vary the magnification, and to keep the camera in accurate focus while the photography is being continued. The camera system is shown diagrammatically in figure 1.

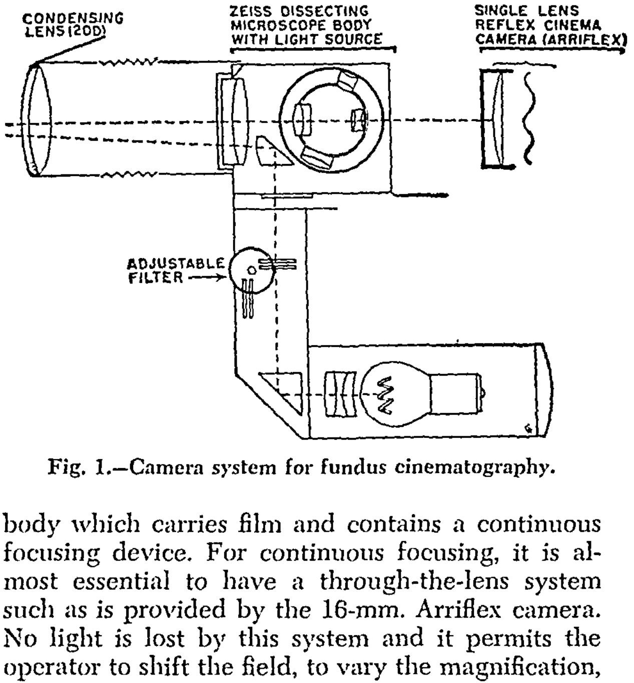
CONDENSING LENS (20D)
ZEISS DISSECTING MICROSCOPE BODY WITH LIGHT SOURCE
SINGLE LENS REFLEX CINEMA CAMERA (ARRIFLEX)
ADJUSTABLE FILTER

Fig. 1.—Camera system for fundus cinematography.

No special film is required. Currently we are using a high-speed color film manufactured by the Ansco Company under the trade name of Super Anscochrome. This can be developed at its usual speed of ASA 100. Satisfactory prints can be made in black and white or color from this film.

The technique of fundus cinematography is similar to that used for still photographs of the fundus. It is essential that the pupil be widely dilated and that the patient cooperate by keeping his head and eyes reasonably stationary. The camera in use with an ambulatory patient is illustrated in figure 2; however, the camera is portable and can be mounted on a standard tripod for use with reclining patients. In the past year film studies have been made of a diversity of conditions. It has been found that the cinematography records satisfactorily nearly all of the functional changes in the retinal vessels which can be observed with a hand ophthalmoscope. In addition, the magnification gained when these changes are projected on the screen frequently brings out alterations in the character of the pulsations which are not discernible even with a binocular ophthalmoscope. Another important observation has been that an amplitude of pulsation or a shift in position of a segment or vessel which may be easily discernible when the movie films are projected may not be evident with serial prints made from the film.

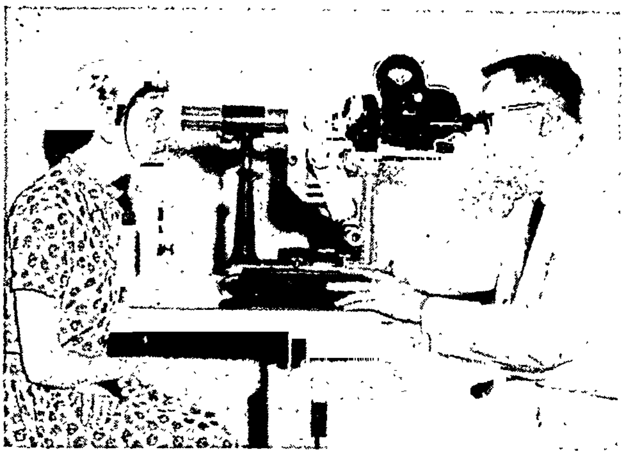

Fig. 2.—Camera system assembled for fundus photography in average ambulatory patient. System can be moved as unit or component parts adjusted separately for varying circumstances.

Films are being made to illustrate variations in the pulsation in normal eyes, in hypertensive disease, in various stages of atherosclerosis, and in disturbances in the carotid circulation. Particularly dramatic changes have been recorded in patients who have cardiac disease with arrhythmias and abnormal pulse pressure. Figure 3 illustrates the vari-

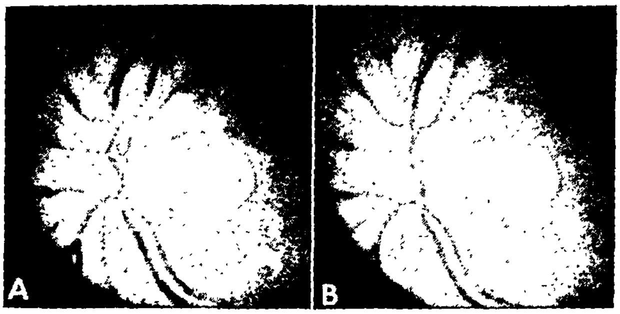

Fig. 3.—Prints made from 16-mm. color film showing that during diastole (*A*) there is filling of veins of optic nerve head, whereas during systole (*B*) transmission of arterial pulsation through vitreous results in marked blanching of veins in center of disk. Patient has aortic valvular insufficiency.

ations in the venous pulsation in the disk which were recorded in the film of a patient with aortic valvular insufficiency. Since the arterial pulsation is transmitted through the vitreous to the retinal veins, the changes seen in the venous system are more dramatic than those in the arterial tree.

Films taken at the University of Oregon Medical School already are in use in student teaching and have proved particularly effective in demonstrating the loss of elasticity in sclerotic disease, in showing such unusual circumstances as the streaming of the red blood cells in the central retinal vessels in central retinal artery occlusion, and in demonstrating the influence of external pressure on the globe as in ophthalmodynamometry.

Summary

A practical camera and technique for retinal cinematography has been designed and is in use at the University of Oregon Medical School to record the functional changes which take place in the retinal vascular system in normal eyes and in the fundus of patients with certain ocular diseases, systemic vascular diseases, or alterations in the carotid circulation. Changes can be demonstrated which are not discernible with ophthalmoscopy or serial still photographs. The movie films have proved to be an excellent aid in the teaching of ophthalmoscopy and in making progress studies in individual patients in several fields of medicine.

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"DIAGNOSTIC SMALL THORACOTOMY" IN IDIOPATHIC PLEURAL EFFUSION

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and
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Exploratory thoracotomy with pleural biopsy was performed in 17 patients who had idiopathic pleural effusions. In each case the operation was done because the usual procedures of thoracentesis, sputum examination, bronchoscopy, and scalene lymph node biopsy had failed to settle the diagnosis. The thoracic cavity was entered by an incision not exceeding 20 cm. in length through the sixth, seventh, or eighth interspace, which permitted exploration of the corresponding half of the thoracic cavity and removal of biopsy specimens. The diagnoses were postpneumonic effusion in seven cases, carcinoma in six, sarcoma in one, tuberculosis in two, and lymphoma in one. Two cases are described in detail to illustrate chronic tuberculous pleurisy in one patient and lymphoblastoma in the other. This method of "small thoracotomy" is suggested for cases in which idiopathic effusions remain unexplained after careful medical and laboratory examinations.

The term pleurisy with effusion has come to be used synonymously with tuberculous pleurisy. This is understandable, as in 30 to 50% of these cases Mycobacterium tuberculosis can be cultured from the thoracentesis fluid. Even higher percentages may be obtained if a guinea pig is inoculated with the fluid. Statistics have shown that roughly 50% of patients with an idiopathic effusion will develop active pulmonary tuberculosis within five years if not treated. While these figures are representative in the younger age groups, such is not the case with older persons. Here, multiple causal factors must be considered and a strong suspicion of primary and metastatic malignancy entertained. It is both unfair and unwise to assume that all sterile pleurisy is due to tuberculosis, especially among older persons.

Other causes of pleural effusion are numerous. However, there is usually sufficient clinical history, when coupled with positive physical findings, to establish the diagnosis.

Although pleural effusion is frequently an initial sign of a disease process, its etiology is often obscure and only recognized with the later appearance of

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From the Surgical Department, Akron City Hospital.

more obvious signs of the disease. In spite of a barrage of laboratory and radiologic examinations, the early diagnosis may be delayed and the proper therapy instituted in a later stage of the disease, when the patient is less responsive to treatment.

Initial diagnostic laboratory procedures for idiopathic pleural effusion should include bacteriological studies of the centrifugated residue of the entire mass of aspirated fluid. Subsequent studies in obscure cases should include specific intradermal tests along with examinations of sputum for pathogens and neoplastic cells. When results of these tests have been negative or inconclusive, bronchoscopy with aspiration biopsy and transbronchial subcarinal lymph node biopsy have sometimes provided the answer. Local excision of a scalene, mediastinal lymph node is easily accomplished with the patient under local anesthesia and can be readily integrated into the program of diagnostic procedures. It has been our policy to employ all of these methods, in addition to repeated examinations of the thoracentesis fluid, in all cases of undiagnosed pleural effusion. If the etiology remains obscure after application of these steps, surgical exploration of the pleural space is both indicated and desirable.

Exploratory thoracotomy is not yet as well accepted as exploratory laparotomy and is erroneously considered by many to be a formidable procedure. Actually, the morbidity and mortality from thoracic exploration is far less than that for abdominal exploration, and its application deserves much more attention than it has been previously given.

The purpose of this report is to present experience with 17 cases of exploratory thoracotomy and pleural biopsy in patients with idiopathic pleural effusion. Two cases are presented in detail and the results of the remaining 15 are summarized.

Procedure

The patients selected for this report were adults of varying ages with idiopathic pleural effusions. Each presented a problem in diagnosis or treatment. All of the patients were thoroughly studied by means of thoracentesis, sputum examination, bronchoscopy, and scalene lymph node biopsy prior to surgery.

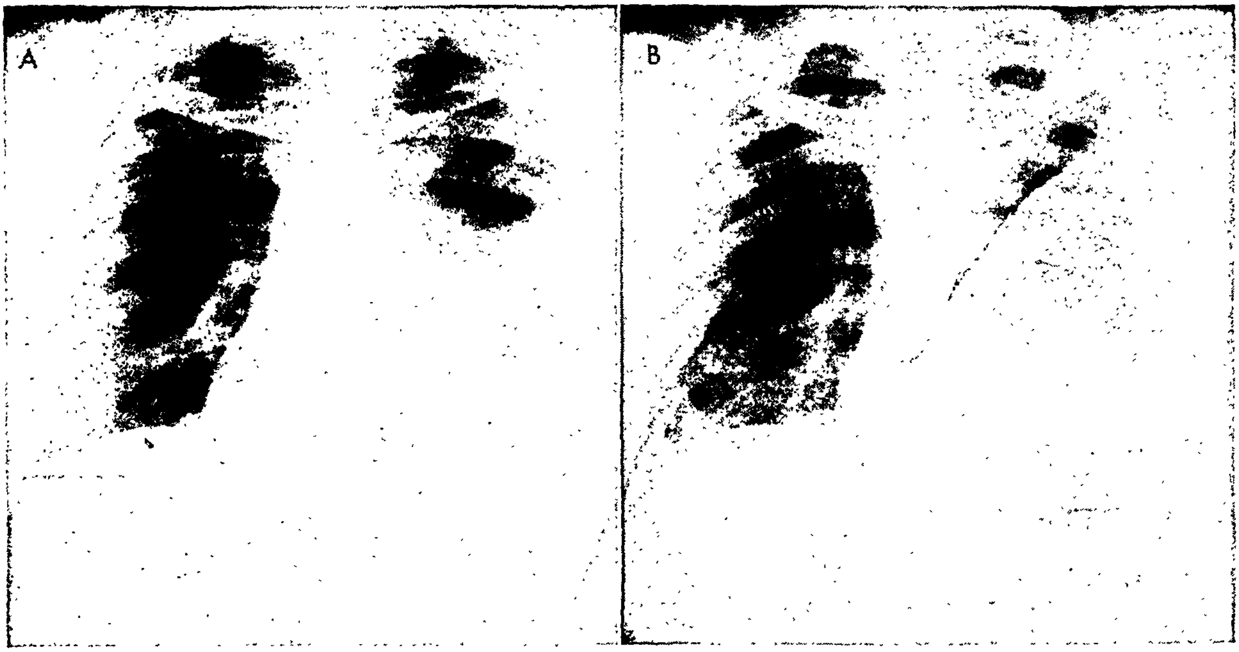

Fig. 1 (case 1).—*A*, posteroanterior view of chest prior to thoracentesis. Note huge left pleural effusion with essentially normal right lung. *B*, posteroanterior view of chest after thoracentesis. Note thickened pleura and obtunded costophrenic sulcus.

The thoracic cavity was entered through the sixth, seventh, or eighth interspace on the appropriate side. The size of the incision was held to a minimum, 6 or 8 in., but in all cases allowed the introduction of the examining hand and a small self-retaining retractor. The entire thoracic cavity could be explored with ease, and adequate biopsy specimens of the involved portions could be taken. In the event that definitive surgical treatment was indicated the incision could readily be extended to permit adequate manipulation of the thoracic contents. Thus, in many cases, exposure was sufficient to establish a diagnosis and yet produce a minimum of postoperative distress. This limited thoracotomy, established in as dependent a portion of the thorax as was consistent with the location of the effusion, was termed a "diagnostic small thoracotomy."

Report of Cases

CASE 1.—A 35-year-old man was admitted to the hospital on Aug. 24, 1957, with complaints of cough and pain in the left side of the chest of one week's duration. He stated that he had had chills and fever on several occasions. Physical examination revealed dulness and absent breath sounds in the left base. X-ray studies substantiated the presence of a massive pleural effusion on the left (fig. 1*A*), and thoracentesis was accomplished. Cultures of this fluid and of the sputum revealed no evidence of M. tuberculosis and the result of the tuberculin skin test was read as negative. After two weeks of therapy and repeated thoracenteses x-ray studies revealed multiple fluid levels and total pneumothorax. Candida and many bacteria were cultured from the chest fluid and sputum, but no evidence of tuberculosis or malignancy was detected. Upper and lower gastrointestinal series were noncontributory. On Sept. 12, 1957, bronchoscopy and scalene lymph node biopsy were undertaken and normal reports returned. Six days later a small thoracotomy was done on the left. The left lung was found to be almost totally collapsed, with a large abscess cavity in the lower lobe. A dense fibrinous peel covered the lung. The pleura was studded with small yellow lesions resembling those of tuberculosis, and there were multiple pockets of yellow fluid present. The lung was decorticated and rose to fill the chest cavity (fig. 1*B*). Biopsy was then performed on a specimen from the pleura (fig. 2) and the chest was closed. The pathologist returned a diagnosis of chronic tuberculous pleurisy and the patient was transferred to a sanitarium for further treatment.

CASE 2.—A 39-year-old woman was admitted to the hospital in August, 1957, with a pleural effusion. She was entirely asymptomatic at that time and knew of no exposure to tuberculosis (fig. 3*A*). Thoracentesis produced about 1,500 cc. of milky fluid resembling chyle. Smears and cultures of this fluid were noncontributory, except that 0 to 1 acid-fast bacilli were reported per high-power field (fig. 3*B*). Results of skin tests for tuberculosis were negative, and the patient showed no further evidence of disease. Bronchoscopy and scalene lymph node examination were done and were reported to be normal. The patient was discharged from the hospital after careful observation during which time the effusion did not recur. She was readmitted to the hospital in November, 1957, with evidence of recurrence of fluid but still completely asymptomatic. Thoracentesis again produced 500 cc. of chylous fluid which was examined and reported as negative for bacteria and tumor cells. The only other significant item in the patient's history was that of removal of a benign rectal polyp three years prior to admission. On Nov. 26, 1957, a small thoracotomy was performed on the left side. Some chylous fluid was again noted in the pleural cavity. The lung, mediastinum, and great vessels appeared normal. There was evidence of enlargement of the aortic lymph nodes, and a tumor mass, roughly 3 by 5 cm., was found retropleurally in the left paravertebral area. This tumor appeared to be in the area of the thoracic duct and apparently invaded the sympathetic chain in this area. A biopsy specimen was taken from the mass (fig. 4) and the chest closed. The pathologist reported lymphoblastomatous transformation of a lymph node with invasion of sympathetic ganglions and nerves.

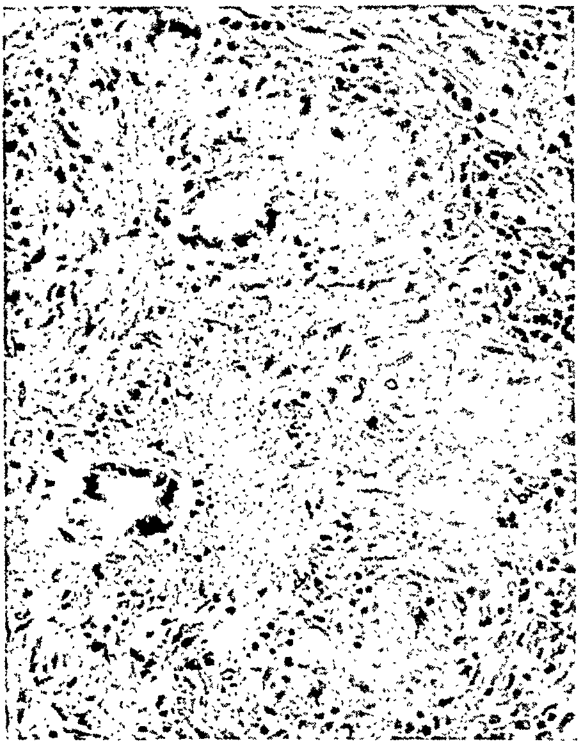

Fig. 2 (case 1).—Low-power view of biopsy specimen. Note central area of necrosis surrounded by multinucleate giant cells. Results of skin tests and laboratory examinations on sputum were negative.

Of 17 consecutive patients, including the 2 whose cases are summarized above, the pathological diagnoses proved by small thoracotomy were postpneumonic effusion in 7; carcinoma in 6; sarcoma in 1; tuberculosis in 2; and lymphoma in 1.

Comment

In 1949 Klassen[1] introduced the term "small thoracotomy" to describe the limited incision employed in the diagnosis of diffuse pulmonary lesions. The utility of this procedure has been increased by adapting it to other undiagnosed intrathoracic lesions. Breckler and co-workers[2] reported on 16 consecutive cases of open pleural biopsy in which an anterolateral incision at the eighth interspace was used. They found that this method had definite advantages over the needle biopsy methods proposed by Heller and co-workers[3] and quickly abandoned the latter. In two cases exploration afforded a diagnosis which could not have been easily made by any other means. Of 10 suspected cases of pulmonary tuberculosis with effusions 9 were proved histologically.

Sutliff and co-workers[4] studied the problem of pleural effusion by open biopsy technique through a 6-in. posterior incision at the eighth interspace. A small segment of rib was removed in each case. In a series of 21 cases 17 were found to be due to tuberculosis, 3 to carcinoma, and 1 to North American blastomycosis. Similar results were reported by Small and Landman[5] who reported on five cases of open pleural biopsy with palpation of the lung and pleura. These were all suspected to be due to tuberculosis, and the diagnosis was proved histologically in all cases by this manner.

Diagnostic thoracotomy for pleural effusion has been performed by Douglass and co-workers[6] who reported on 21 cases. The authors described the relative merits of the procedure and concluded that thoracotomy was a valuable aid in the diagnosis of these effusions. Of the 21 cases presented, 6 were found to be caused by neoplasm, 1 was attributed to trauma, 5 showed histological evidence of tuberculosis, 7 were due to other inflammatory processes, and in 2 the cause was indeterminate.

Exploratory thoracotomy is not a new thing, but some trepidation still exists when surgeons suggest thoracotomy as a diagnostic procedure. Conservative medicine is not always the best medicine, however, and many hospital days and much morbidity can be saved when guesswork is eliminated. In our hospital idiopathic effusions are treated conservatively, at first, but when we have failed to arrive at a tenable diagnosis after careful medical and laboratory examination we suggest small thoracotomy. Mortality and morbidity are quite low. The diagnosis and prognosis are established and definitive therapy is not infrequently carried out during employment of such a diagnostic small thoracotomy for pleural effusion.

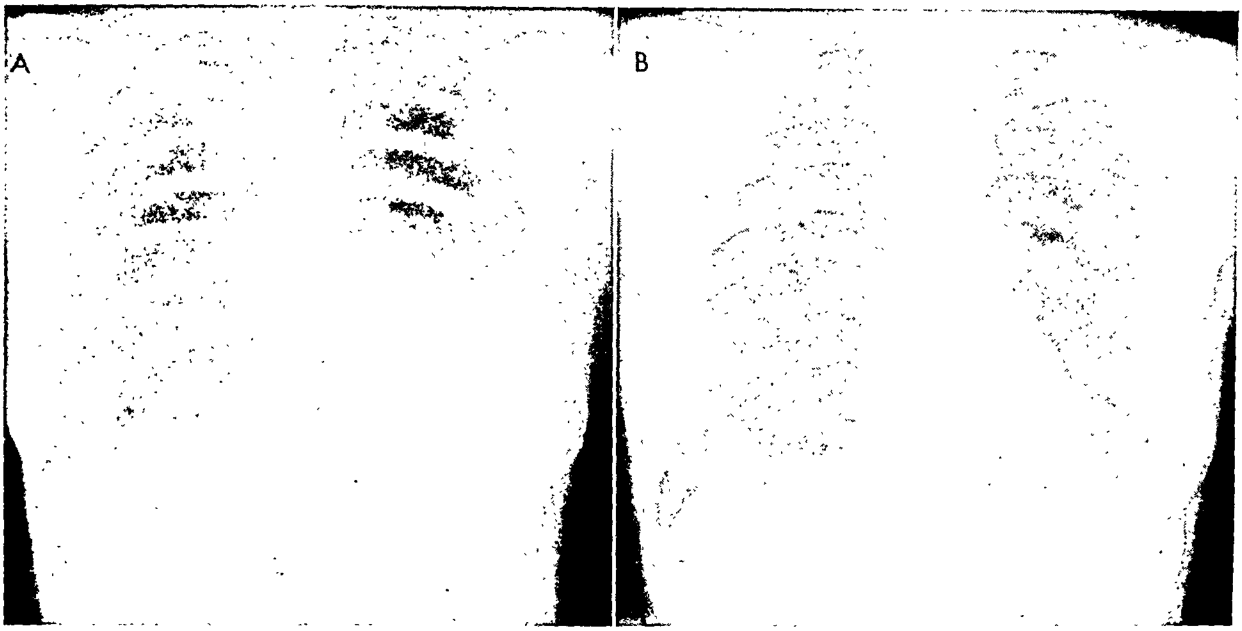

Fig. 3 (case 2).—*A*, posteroanterior view of chest prior to thoracentesis. Note large left pleural effusion and otherwise normal appearance. Patient was entirely asymptomatic. *B*, posteroanterior view of chest after thoracentesis produced 1,500 cc. of chylous fluid. Results of skin tests for tuberculosis were negative.

Summary

The pathological diagnosis was established by small thoracotomy and biopsy in 17 consecutive patients with idiopathic pleural effusion. This

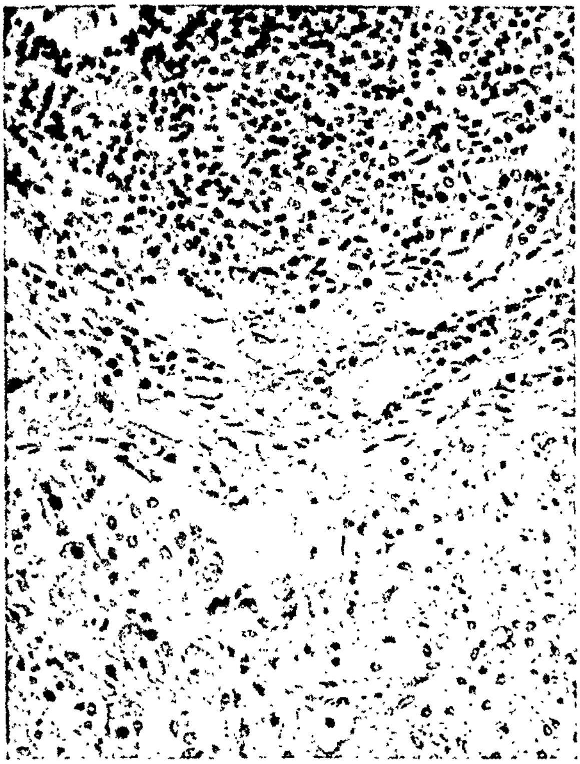

Fig. 4 (case 2).—Low-power view of biopsy specimen. Note extensive small cell infiltration of specimen. Large cells in lower left are cell bodies of sympathetic ganglions in this area. There was no histological evidence of tuberculosis.

method has definite advantages over other methods in that the entire disease area can be observed, palpated, examined by biopsy, and, where practical, treated. Many hospital days and much morbidity can be eliminated when the etiology of the effusion is ascertained and definitive therapy is started. The establishment of prognosis is an invaluable by-product of the procedure.

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Histological and laboratory examinations were done by the Department of Pathology, Akron City Hospital, under the direction of Lloyd Catron, M.D. Photographs were made by Mr. John A. Muldowney.

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ATTITUDES TOWARD GROWING OLDER.—This study of attitudes toward aging is based upon interviews with a sample of 625 men and women aged 40 to 70 residing in the metropolitan area of Kansas City. The group constituted a random sample of individuals (not married couples) drawn by area-probability technics and stratified by age, sex, and social status. The sample was approximately equally divided between men and women as well as among persons of each of four social-class levels. . . . Data were gathered in connection with a larger study, the Kansas City Study of Adult Life. In an extensive interview . . . a number of questions were asked regarding attitudes toward the present and toward the future. . . . There was a striking consistency in the content of responses about the future. For those persons expressing negative or contingent attitudes toward the future, the fear of some form of dependency is paramount. They say: "Growing old is terrible, because somebody has to take care of you," or "I don't mind growing old as long as I don't become a burden to others." Dependency in turn is always seen as having two sources—loss of income and loss of health. Seldom is one mentioned without the other. Fear of death is never alluded to, nor is fear of social isolation. Illness, blindness, and deafness are seen not as threats to bodily integrity, but as states involving dependence upon others. This triad—dependency, loss of health, and loss of income—was the only theme to occur with any frequency. It is of special interest that the incidence of this response was approximately the same for men as for women, for the different social classes, and for people at all ages. Since the 40-year-old mentions the dependency triad as frequently as does the 60-year-old, it appears that he interprets the question about growing older as referring to a period of "being aged," and not to the near or relatively near years of the 50s and 60s. Thus, for all people, "becoming older" does not appear problematic—it is "being old" that has meaning.—B. L. Neugarten, Ph.D., and D. C. Garron, Attitudes of Middle-Aged Persons Toward Growing Older, *Geriatrics,* January, 1959.

NEW ANTIBODY (ANTI-Rh^B) RESULTING FROM BLOOD TRANSFUSION IN AN Rh-POSITIVE PATIENT

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Clinicians are well aware that erythroblastosis fetalis (hemolytic disease of the fetus and newborn) results from an incompatibility of the blood of the baby for the mother's serum, while hemolytic transfusion reactions are due to incompatibilities between patient's and donor's bloods. Many blood factors exist, and, therefore, many different kinds of incompatibilities are possible. In fact, it is hardly possible to transfuse blood that is identical in all its blood factors with that of the patient. To do so would necessitate that some 150,000 varieties of blood be kept constantly available, whereas, at present, blood banks stock only eight different varieties. It is the purpose of this paper not to elaborate on the details of this complicated immunohematological subject but, rather, to call attention to and to clarify one puzzling situation.

As explained in a previous report,[1] in recent years a number of cases have been encountered in which patients who had had hemolytic transfusion reactions and mothers of erythroblastotic babies were found to be Rh$_o$-positive yet had antibodies in their serum resembling anti-Rh$_o$ in specificity. This constituted a paradox, since, theoretically and in practice, it had been found that only Rh$_o$-negative persons can be sensitized to the Rh$_o$ factor. Closer study then disclosed that the antibodies in these patient's serums were actually not identical with Rh$_o$, since they failed to react with the red blood cells of the patients as well as cells from certain other rare Rh$_o$-positive persons. Comparison of the antiserums from different Rh$_o$-positive patients so sensitized showed that the antibodies differed not from anti-Rh$_o$ but from one another. Therefore, they had to be assigned distinctive symbols, and we have used the designations anti-Rh^A, anti-Rh^B, anti-Rh^C, etc., in rotation for the antibodies we studied. It is now clear that in the Rh agglutinogens associated with factor Rh$_o$ there are multiple blood factors other than Rh$_o$, namely, Rh^A, Rh^B, Rh^C, etc. (The Rh agglutinogens include all agglutinogens having in common factor Rh$_o$, namely, agglutinogens Rh$_o$, Rh$_1$, Rh$_2$, and Rh$_z$). In certain rare Rh-positive persons, one or more of these factors may be lacking, and such persons can be sensitized to the missing factor or factors. As has been explained, the resulting antibody which is formed, anti-Rh^A, anti-Rh^B, or anti-Rh^C, as the case may be, simulates anti-Rh$_o$ in specificity.

A woman, aged 57, received four blood transfusions at various times during a period of three months before, during, and after surgery. Before each transfusion the prospective donor's blood was shown to be compatible by an unusually elaborate series of tests; yet the first two transfusions were followed by chills and fever, presumably because of some unrecognizable incompatibility. The results led the authors to the conclusion that in Rh-positive blood, associated with the Rh$_o$ factor, there are other blood factors which they designate Rh^A, Rh^B, Rh^C, etc. The complications in this case could be explained when it became possible to demonstrate in the patient's serum the presence of a new antibody, which they designate as anti-Rh^B.

Wiener and co-workers[2] studied the serum of a type Rh$_1$rh mother who gave birth to an erythroblastotic type Rh$_1$rh baby. To the antibody in the mother's serum they assigned the symbol anti-Rh^A. Two of us (L. J. U. and A. S. W.) have reported the results of extensive studies[3] on blood factor Rh^A and a similar case involving twin erythroblastotic babies.[4] To the factor in the latter case the symbol Rh^C has been assigned and to the antibody anti-Rh^C. The present paper deals with a hemolytic transfusion reaction in an Rh$_o$-positive patient caused by Rh sensitization. To the antibody in this case the symbol anti-Rh^B has been assigned.

Report of a Case

The patient, a 57-year-old Italian woman weighing 103 lb. (46.7 kg.), was hospitalized in August, 1957, as a patient of Dr. L. M. Rosati, with the diagnosis of Laennec's cirrhosis, fatty stage. She had had three children, all living and well. There had been no miscarriages or stillbirths. Previous operations were appendectomy and uterine suspension, but there was no history of previous blood transfusions. Her present complaint was pain in the right upper quadrant of the abdomen.

Physical examination revealed an enlarged, firm, but not tender liver and spleen, both being palpable 3 fingerbreadths below the costal margin. The patient did not have jaundice. The results of both cholecystography and cholangiography were negative. Laboratory findings were as follows: hemo-

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globin level 11.9 Gm.%; red blood cell count 5,600,000 per cubic millimeter; white blood cell count, 5,600 per cubic millimeter, with polymorphonuclear cells 51%, lymphocytes 38%, monocytes 2%, and eosinophils 9%; total protein level 7.4 Gm. per 100 cc., with albumin-globulin ratio 1.6; prothrombin time 13 seconds; total bilirubin level 0.7 mg. per 100 cc.; and sulfobromophthalein retention 16% (normal up to 5%).

While in the hospital the patient was afebrile. No blood transfusions were administered, and the only treatment given was a diet supplemented with vitamins. She was discharged from the hospital but readmitted two and one-half years later because of hematemesis and tarry stools. Her liver and spleen were now palpable 5 fingerbreadths below the costal margin. X-ray examination revealed esophageal varices. Her hemoglobin concentration on the day of admission was 7.8 Gm.%. The examination of her blood showed it to be group B, Rh-positive. Blood transfusion was ordered and 1,000 cc. of group B, Rh-positive blood administered. Twenty days later a second transfusion was given, 500 cc. of group B, Rh-positive blood. Fifty-one days after admission, a portacaval shunt operation and cholecystectomy were performed. During the operation an ice mattress was used and the patient's temperature lowered to 95 F (35 C). While under anesthesia in the operating room and recovery room, she was given a third transfusion of 1,500 cc. of group B, Rh-positive blood. At the time of operation, the portal pressure was 480 mm. of saline solution, indicating portal hypertension. After the shunt was performed, the portal pressure dropped to 225 mm. of saline solution. Biopsy of the liver disclosed portal cirrhosis. Four days postoperatively, she received a fourth transfusion, this time of group B, Rh-negative blood. She was discharged from the hospital three months after admission.

Results of Blood Tests

The routine procedure for crossmatching used at this hospital includes both major and minor crossmatching, as well as tests on a mixture of patients' serum with patients' own cells carried out by three different methods, namely, saline agglutination, albumin-plasma conglutination, and antiglobulin techniques. In addition to these pretransfusion compatibility tests, sensitivity tests are carried out to detect any atypical antibodies which may be present in the serums of patient and donor. For these sensitivity tests, as test cells, a pool of type Rh_zRh_0 cells, both untreated and treated with ficin, is used with the saline agglutination and antiglobulin methods. The latter method, namely, ficinated-cell antiglobulin, was first described by one of us (L. J. U.) [5] and is the most sensitive of all. Prior to each blood transfusion, a freshly drawn specimen of the patient's blood is obtained for use in the pretransfusion tests.

Before the first blood transfusion was given to this patient, the results of all the tests were negative and the donors' bloods were considered to be compatible and were, therefore, administered. Nevertheless, the patient experienced a post-transfusion chill and her temperature rose to 104 F (40 C). Since no in vitro incompatibility could be demonstrated, since there was some post-transfusion rise in the hemoglobin concentration and erythrocyte count, and since there was neither hemoglobinuria nor any immediate rise in blood bilirubin concentration, this reaction was interpreted as pyrogenic in nature. When the patient's serum bilirubin concentration rose two weeks later and she had mild jaundice, it was natural to ascribe this to the diagnosed cirrhosis of the liver, especially since the question of some degree of jaundice had been raised at the time of admission. Also considered at this time were the possibilities of hepatitis superimposed on cirrhosis of the liver, autohemolytic anemia, and hypersplenism.

About three weeks after admission, the second blood transfusion was given, after the donor's blood was shown to be serologically compatible by all the tests previously mentioned. It is interesting that a weak reaction was reported in the sensitivity tests when the patient's serum was screened for atypical antibodies, but only by the highly sensitive ficinated-cell antiglobulin method. The blood found compatible by the crossmatching tests was administered. This second transfusion was also followed by a severe chill and fever. A direct antiglobulin test on the patient's red blood cells then showed a positive result of 1+, but this was interpreted as due to autoantibodies because a similar 1+ reaction was obtained at this time when the patient's serum was tested against ficinated type rh, type rh′ and type rh″ cells. In retrospect, it seems more probable that the direct antiglobulin reaction was due to surviving donor's cells coated with the offending antibody in the patient's serum. The positive result of the direct antiglobulin test persisted for at least nine days after this second transfusion and possibly longer, since the test was not repeated until another month had elapsed, at which time the result was again positive. From the results of the blood bilirubin determinations and blood cell counts (table 1), the major portion of the blood given at the second transfusion must have been eliminated promptly, in contrast with the slow elimination of the blood of the first transfusion, and the balance was eliminated more slowly, as indicated by the persistence of the positive direct antiglobulin reaction—unless the latter was, in fact, due to autoantibodies. Again, no hemoglobinuria occurred and kidney function was apparently unimpaired.

One month later, prior to operation, the same crossmatching tests were again carried out and in vitro compatible blood selected. In these tests, made by a technician on duty at night, no unusual reactions were noticed. No clinical symptoms were observed after this transfusion, but the patient was under refrigeration anesthesia, which could have suppressed any reaction which might otherwise have occurred. There was a post-transfusion rise in temperature, but this could be ascribed to the operation itself. The blood administered at this transfusion was promptly eliminated, because, after an initial rise, the hemoglobin concentration became lower than before transfusion and there was a simultaneous sharp rise in serum bilirubin concentration. Again, there was no impairment of kidney function, although the nurse noted on the chart the passage of "dark" urine.

TABLE 1.—*Clinical Laboratory Findings*

Date*	Hemoglobin Level, Gm. %	Erythrocyte Count, Millions/Cu. Mm.	Bilirubin Level, Mg./100 Cc.	Comment
3/ 7	7.8		1.05	Pretransfusion
3/17				1,000 cc. of group B, Rh-positive blood given
3/26	8.8	3.3	1.72	
4/ 2	7.8		7.9	Jaundice
4/ 6				500 cc of group B, Rh-positive blood given
4/ 8	6.4	2 39	16.5	
4/11	7.5	2.9	15 2	Direct antiglobulin test result positive
4/15			5.6	Direct antiglobulin test result positive
4/24	8.0		3.9	
4/29	9 8			
5/ 7	10.5 (post-transfusion)		4.4	1,500 cc. of group B, Rh-positive blood given in operating room and recovery room
5/ 9	6.8		30.2	
5/11	6.4		19.6	500 cc. of group B, Rh-negative blood given
5/14				Direct antiglobulin test result positive with admixture of negative cells
5/17	6.0			
5/19	7.2			
5/28	9.8		10.22	Reticulocytes 9.2%
6/10	9.4		10.47	
7/10				Direct antiglobulin test result negative

*In a few instances, for compactness, tests performed within a few days of one another are recorded as if they were done on same day.

After the operation, when a fourth transfusion was requested, crossmatching tests for the first time gave a 1+ reaction by the antiglobulin technique. This occurred in the minor match as well as in the major match, and the same degree of clumping was observed by the antiglobulin technique in a mixture of the patient's cells with her own serum, so that the reaction obtained could be attributed to autoantibodies. However, a 2+ result in the sensitivity test for atypical antibodies in the patient's serum, with use of pooled Rh_2Rh_0 test cells by the ficinated-cell method, and a 3+ result by the ficinated-cell antiglobulin method caused the technician to withhold blood for transfusion. When the crossmatching tests were carried out with Rh-negative blood no incompatibility was detected, so for this transfusion group B, type rh blood was used and no untoward reaction resulted. After this, the patient's condition improved and she was then discharged from the hospital.

TABLE 2.—*Illustrative Reactions of Serums from Three Sensitized Rh-Positive Patients**

	Antiserums			
Cells	Anti-Rh_0†	Anti-Rh^A (Case 1)	Anti-Rh^B (Case 2)	Anti-Rh^C (Case 3)
Rh_1^{ab} rh (case 1)	+	0	0	+
Rh_2^{b} rh (case 2)	+	+	0	+
$\mathfrak{R}h_2^{c}$ rh (case 3)	+	+	+	0
$\mathfrak{R}h_0^{ac}$‡	+	0	+	0
"Standard" Rh	+	+	+	+

* Data from Unger and Wiener.[3a]
† Serum from a Rh_0-negative person sensitized by blood factor Rh_0.
‡ Rh-positive person, not sensitized.

The patient's blood was then studied by two of us (L. J. U. and A. S. W.). Her blood group proved to be B, type Rh_2rh, and in her serum a new antibody was found. Differential agglutination tests showed no evidence of survival of donors' cells from the transfusions she had received. To the particular antibody in the serum of this patient was assigned the symbol anti-Rh^B. Table 2 shows some of the differences in specificity of anti-Rh^A, anti-Rh^B, and anti-Rh^C. That the antibody in the present patient's serum is not anti-Rh^A or anti-Rh^C follows from the fact that the patient's red blood cells, with which her antibody does not react, react with anti-Rh^A serum and also with anti-Rh^C, and to approximately the same titer as with "standard" Rh-positive red blood cells.

TABLE 3.—*Titration Results of Patient's Serum (Anti-*Rh^B*)*

	Rh-Hr Type of Cells Used and Titer, Units*								
	1†			2‡			3§		
Method of Titration	Rh_1-rh	Rh_2-rh	rh	Rh_1-Rh_1	Rh_2-rh	rh	Rh_1-Rh_1	Rh_2-Rh_2	rh
Saline agglutination	0	0	0	0	0	0	0	0	0
Albumin-plasma conglutination	0	0	0	16	16	0	64	64	0
Antiglobulin	0	0	0	16	16	0	96	96	0
Ficin-treated cell	128	48	4	64	32	2	256	256	2

* Units = reciprocal of highest dilution of serum giving 1+ reaction (all test cells used were group O).
† Blood specimen drawn prior to last transfusion.
‡ Blood specimen drawn one month after last transfusion.
§ Blood specimen drawn three months after last transfusion.

Table 3 gives the results of titrations of the patient's serum. The initial titrations were carried out on serum obtained after she had received the second blood transfusion. At that time, her serum failed to show clumping by the saline agglutination, albumin-plasma conglutination, and antiglobulin methods. The fact that the antibody reacted only by the ficinated-cell method explains the failure of the technician to detect the offending antibody by the crossmatching tests, since the ficinated-cell method has never previously been used for compatibility tests. The second set of titrations was carried out with the patient's serum obtained after she had received the third blood transfusion, when the offending antibody was first detected in crossmatching tests. The third set of titrations was carried out on the patient's serum obtained approximately one month after her discharge from the hospital, and the results were similar to those of the second titration except that the titer values were higher, namely, 256 units. The titer of 2 units with group O rh cells, as previously noted, persisted. Seven months after the third titration another titration was carried out. At this time, although the titer values had fallen appreciably, the reaction for type rh cells persisted in a titer of one unit.

Tests were carried out on blood of members of the patient's family in order to investigate the hereditary transmission of her unusual agglutinogen Rh_2^{b}. Unfortunately, her husband could not be located, while her three sons all proved to have standard Rh-positive blood, that is, blood which has factor $\mathbf{Rh}_0$ and all the associated blood factors, $\mathbf{Rh}^A$, $\mathbf{Rh}^B$, and $\mathbf{Rh}^C$. The blood groups of her three adult sons (36 years, 35 years, and 30 years of age), were A_1B MN $\mathrm{Rh}_2\mathrm{Rh}_2$, A_1B N $\mathrm{Rh}_z\mathrm{Rh}_0$, and A_1B N $\mathrm{Rh}_1\mathrm{rh}$ respectively. While throwing no light on the heredity,[6] these results suggest that the original source of the patient's sensitization to the $\mathbf{Rh}^B$ blood factor might have been her pregnancies. These pregnancies probably acted as primers so that a latent sensitization was present when the patient was admitted to the hospital and the transfusions then stimulated the appearance (or possible reappearance) of the isoantibodies in the serum.[7]

Comment

From the onset, the findings in this case were puzzling and misleading and presented a complex clinical picture. The patient had portal cirrhosis, esophageal varices, and massive hemorrhages requiring surgical treatment and blood transfusion therapy. An enlarged spleen, enlarged liver, and absence of renal impairment or hemoglobinuria understandably caused the jaundice when it developed to be attributed to the primary disease rather than to the transfusion. The laboratory findings, too, were puzzling, in that an elaborate and acceptable pretransfusion crossmatching routine at first disclosed no serologic incompatibility between her blood, which was group B, Rh-positive, and that of blood of group B, Rh-positive donors. It was, therefore, reasonable to conclude that the post-transfusion reactions were simply pyrogenic.

There was no history of previous blood transfusions, yet, as a result of previous pregnancies, the patient was probably already isosensitized when admitted to the hospital. At the time of the first transfusion, the titer of the antibody was too low to be detected by any presently known crossmatching test but a chill and fever resulted. After repeated transfusions, the isoantibody became demonstrable and the incompatibility became detectable, so that further transfusions of Rh-positive blood were avoided. The offending new antibody was then identified, and to it was assigned the symbol anti-$\mathbf{Rh}^B$. We have observed that examples of anti-$\mathbf{Rh}^A$, anti-$\mathbf{Rh}^B$, and anti-$\mathbf{Rh}^C$, which are the only examples now available, all give the strongest reactions by the ficinated-cell and ficinated-cell antiglobulin methods. Yet these two methods have not been used previously for crossmatching tests. This case demonstrates the need to incorporate in the routine pretransfusion procedure sensitivity tests carried out with the patient's and donor's serum. This was suggested in 1954.[8] It further shows that, occasionally, bloods may appear to be compatible by the accepted routine procedures for crossmatching and that sensitivity tests may also fail to reveal the presence of an atypical antibody and, yet, transfusion may be followed by reaction. If agglutination is observed in sensitivity tests by the ficinated-cell or ficinated-cell antiglobulin methods, blood transfusion should be withheld until crossmatching tests have been carried out by the two new methods recommended in this paper. The commonly used ficinated-cell technique requires a considerable quantity of blood; therefore, the "short" method devised by one of us (A. S. W.) is recommended.

Summary

An Rh-positive patient sustained a hemolytic reaction after transfusions of seemingly compatible Rh-positive blood. In her serum, finally, an antibody was detected, closely simulating anti-$\mathbf{Rh}_0$ in specificity but differing in that it failed to react with her own red blood cells and those of certain other Rh-positive persons. Since the antibody also proved to be different from anti-$\mathbf{Rh}^A$, previously described by Wiener and Geiger, it has been assigned the symbol anti-$\mathbf{Rh}^B$. It is now known that in Rh-positive blood associated with the $\mathbf{Rh}_0$ factor there are multiple other blood factors, such as $\mathbf{Rh}^A$, $\mathbf{Rh}^B$, and $\mathbf{Rh}^C$. Physicians should watch for those rare Rh-positive patients whose blood lacks one or more of the associated factors, because such persons can be sensitized to the missing factor with resulting clinical complications, such as a hemolytic transfusion reaction or the birth of an erythroblastotic baby.

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In this paper the recommendation of the Committee on Medicolegal Problems of the American Medical Association has been adopted to use regular type for symbols for agglutinogens and phenotypes, boldface type for symbols for blood factors and their corresponding antibodies, and italics for symbols for genes and genotypes.

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SYNDROME OF MINIMAL CEREBRAL DAMAGE IN INFANCY

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Among the chronic diseases, the neuropsychiatric disabilities are probably the most costly in terms of loss of productivity, the need for provision of treatment and care, the chronicity, and the disruption of family life. Two major problems in this connection are the elucidation of etiological factors and the identification of deviation early in life so that plans for education and management can be made.

Some time ago we constructed the hypothesis of a "continuum of reproductive casualty" which has been investigated in a series of retrospective and anterospective epidemiologic studies. According to this hypothesis, there is a lethal component of cerebral damage which results in fetal and neonatal deaths and a sublethal component which gives rise to a series of clinical neuropsychiatric syndromes depending on the degree and location of the damage. We have found that these abnormalities range from the more obvious disabilities, such as cerebral palsy,[1] epilepsy,[2] and mental deficiency,[3] through the learning and behavioral difficulties, such as reading disabilities,[4] tics,[5] and the behavior disorders of childhood,[6] probably as a result of cerebral disorganization after minimal cerebral damage. The retrospective investigations have indicated that three prenatal and paranatal factors appear to be most highly associated with the components of this continuum, namely, prematurity, toxemia, and bleeding during pregnancy. In the retrospective study of children with behavior disorders, this association was found to be particularly high in the hyperactive, confused, and disorganized group. In this paper we propose to draw on one of the major anterospective studies, that of premature infants,[7] which supports the hypothesis by showing an increase in the brain damage in such infants, in order to discuss the clinical aspects of the syndrome of minimal cerebral damage in infancy and its prognostic importance in identifying infants who might later develop behavioral and learning difficulties.

If the hypothesis is correct, and those infants who have abnormal neurological findings early in life are the ones who present childhood behavior disorders, there is need for a more refined tool than the usual neurological examination of the infant and young child, since this is geared toward detecting gross defects, such as congenital anomalies of the central nervous system and advanced, expanding lesions of the brain. The lesser degrees of neurological abnormality are not readily defined by this procedure, and the minor abnormal neurological patterns are looked on merely as the "clumsiness" or "immaturity" that is described in all children. Because of the inextricable interrelationship of developmental maturational level and neurological functioning, a knowledge of the developmental patterns in infancy and early childhood defines the degree of so-called clumsiness to be expected at any given age and, furthermore, delineates what part of the body is involved and in what types of activities. Such knowledge also indicates whether the personal, social, and emotional response of the child is appropriate to his age, making it possible to explain deviant behavior by environmental factors; widely discordant responses would intensify the search for organic disease.

Examination of 500 premature and 492 full-term infants at 40 weeks of age indicated that there is a continuum of cerebral damage ranging from severe abnormalities, such as cerebral palsy and mental deficiency, to minimal damage. All degrees of involvement increased as the birth weight decreased. The number and severity of abnormal neurological and behavior patterns recorded varied directly with the severity of the clinical neurological diagnosis. The component items for a diagnosis of minimal cerebral damage in infancy are described. Findings of adaptive functioning at 40 weeks were found to be well correlated with maturity levels at 3 years of age and therefore have predictive value. Behavior problems in children have been ascribed to tension in their mothers, but the likelihood that an infant with difficulties produces tension in his mother needs serious consideration.

The syndrome of minimal cerebral damage as we define it is manifested by minor but clearly defined deviations from the normal neurological and behavioral developmental patterns, usually with more or less complete compensation by 15 to 18 months of age, as determined by the standard neurological examination. These developmental abnormal neurological signs persist well into the preschool period but require special techniques and a knowledge of maturity to elicit and interpret them. The syndrome is important in the early identification of expanding lesions of the brain, in following the progress of a child with a neurological abnormality, and in identifying those infants who, because of their cerebral disorganization, might be more apt to develop neuropsychiatric disorders later in childhood.

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Method of Study

The present report is based on the examination of 500 premature and 492 full-term control infants who were evaluated as part of a study of premature infants conducted in Maryland since 1952. The details of the selection of the sample, the success of the follow-up study and completion of the examination, and the examination procedures have already been described.[7] These infants were all residents of Baltimore and were examined at an average age of 40 weeks. In premature infants, the chronological age was corrected for the estimated amount of prematurity. In considering the possibilities of bias, it is important to emphasize that the examiner, in the great majority of instances, had no knowledge at the time of the examination about whether the infant was premature or was a full-term control infant.

The following procedures were used in gathering information relative to the subject matter of this report: The details regarding the behavior in the first month of life, intercurrent illnesses, the occurrence of convulsive seizures, and the emotional behavior of the child were obtained from the mother at the time of the examination. For those infants examined in the office, someone other than the pediatrician, for the most part one nurse on the study staff, interviewed the mother. When the infant was examined at home or elsewhere, the pediatrician obtained the history after the examination was completed and recorded. An estimate of the mother's behavior in terms of self-assurance and tension was made by either the nurse or the physician at the time the history was taken. The neuropsychiatric developmental examination of Gesell and Amatruda [8] and a physical examination were done by the pediatrician, and, among other things, a diagnosis of neurological status and a prediction of intellectual potential were made.

The neurological status is an estimate of the integrity of the central nervous system as this is manifested by the absence or presence of impairment in neuromotor functioning and deviations in muscle tonus and control. It is expressed in terminology, appropriate to the field of infant neurology, which indicates the extent of departure from normal and comprises five categories. Those infants who are called normal are without abnormal neurological findings, while those in the "possible minimal damage" category have deviations from normal patterning so minor that they are considered to be of no clinical significance and, for summary purposes, this group is added to the normal group. The syndrome of minimal damage has already been defined. Another group, "possible cerebral palsy," includes infants who have signs and symptoms which would warrant a diagnosis of cerebral palsy had they been observed in an older child. However, although clinical experience with the examination technique indicates that most infants with this degree of abnormality at 40 weeks of age eventually compensate completely and have no detectable neurological residuals, cerebral palsy can not be ruled out definitively. The final group, with overt abnormality, shows gross deviations from normal neurological patterning of sufficient degree to raise serious questions about future development. These are infants who would be expected to show abnormal neurological patterns detectable by a standard neurological examination in the later preschool or early school period.

Findings

The distribution of the neurological diagnoses in the premature and the full-term control groups is shown in table 1; this table indicates that, as the birth weight decreases, the amount of damage increases. Of those infants whose birth weight was 1,500 Gm. (3½ lb.) or less, 26.3% were in the possible cerebral palsy or overt neurological abnormality groups, the comparable figures for the larger premature infants and the full-term control infants being 7.2 and 1.6% respectively. When data in the premature group are adjusted for the birth weight distribution of the infants, the incidence of the serious neurological abnormalities in the total premature group is 8.2%. In the minimal damage group were 22.8% of the very small premature infants, 16.0% of the larger premature infants, and 10.0% of the full-term control infants. Again, the rates are significantly higher in the premature infant

TABLE 1.—*Neurological Status of Premature and Full-term Control Infants at Examination at Forty Weeks of Age, Baltimore, 1952-1953*

Weight Group, Gm.	No. of Infants	Normal, %	Possible Minimal Damage, %	Minimal Damage, %	Possible Cerebral Palsy, %	Overt Abnormality, %
Premature						
1,500 or less...	57	29.9	21.0	22.8	14.0	12.3
1,501-2,500	443	63.6	13.1	16.0	5.6	1.6
Subtotal, adjusted for weight distribution ...	500	62.0	13.5	16.3	6.1	2.1
Control, 2,501 or more	492	78.0	10.4	10.0	1.0	0.6
Total	992	68.9	12.2	13.4	3.8	1.7

Analysis of the behavior patterns in the first month of life and up to the time of the examination, about which information was obtained on the basis of the history, indicates that, in general, as the neurological abnormality increases the incidence of an abnormal pattern increases. In the first month of life there are significant differences among the neurological groups for difficulty in sucking, hypotonicity, and hypertonicity. Up to the time of the examination there are significant differences in the incidence of twitching and convulsions, in the number with feeding problems, in the percentage of infants described as usually cranky and unwilling to play alone, and in the number afraid of strange things and situations. Also, the percentage of mothers described as tense and uncertain increases as the degree of neurological abnormality increases.

In addition to this general analysis of historical material, a detailed study was made of 46 individual neurological patterns in order to see the actual relationship between the amount of abnormality recorded and the clinical neurological diagnosis made, thus defining the diagnostic criteria more precisely. The neurological patterns were rated as 0, or normal, and 1, 2, and 3 +, representing varying degrees of abnormality. For each of the neurological categories the average score of all of the cases for the entire 46 patterns was obtained. The results shown in table 2 indicate that the mean score increases significantly as the severity of the estimate of neurological status increases. The mean score for the normal group is 3.9, for the possible minimal damage group 11.1, for the minimal damage group 20.9, for the possible cerebral palsy group 24.8, and for the overt abnormality group 27.7.

Further analysis of the individual items was done to determine the correlation of a given pattern with the remainder of the patterns and to rank them as to their importance in distinguishing between the neurological diagnostic categories. Only 16 of the 46 items do not differentiate significantly between the normal and the minimal cerebral damage groups. In most cases, either the pattern was one indicative of more serious abnormality, such as persistence of a tonic neck reflex or the presence of athetosis, or the total number of infants with that behavior was too small. Only 4 of these 16 patterns do not differentiate at all over the five diagnostic categories, primarily because the total number of infants with the pattern was too small. The items which have the highest correlations with the remainder are those in areas which one might expect at 40 weeks of age: difficulty in the use of the hands and changes in reflexes or muscle tone. (The complete listing and distribution of the individual behavior patterns among the neurological diagnostic categories is available from the authors, but the table is too detailed to be given here.)

TABLE 2.—*Mean Score on Individual Neurological Patterns According to Diagnosis at Forty Weeks of Age, Baltimore, 1952-1953*

Neurological Status	No. of Cases	Mean Score	Standard Deviation
Normal	680	3.9	1.4
Possible minimal damage	121	11.1	5.8
Minimal damage	137	20.9	7.5
Possible cerebral palsy	37	24.8	8.4
Overt abnormality	17	27.7	11.5

Comment

Of utmost importance to the interpretation of the meaning of these findings is the relationship of the behavior in infancy to that found later in life. Contrary to most previous reports,[9] our findings indicate that, when the developmental examination of Gesell and Amatruda is used as a clinical neurological tool by a physician trained in the techniques, it is possible to predict the later development.[10] In contrast to reports in the literature of correlations ranging from 0.2 down to small negative correlations, when the maturity levels of approximately 300 children examined at 3 years of age were correlated with the findings at 40 weeks, a correlation of 0.75 was found for those infants called abnormal at 40 weeks of age, while a correlation of 0.5 was found in the total group.

As would be predicted by the definitions of the neurological status categories, there is a shift toward a diagnosis of less severe involvement with increasing age. The ultimate answer to the major question of the prognostic value of the syndrome of minimal cerebral damage awaits further follow-up examination of these infants and cannot be given at the present time. When these children enter school it will be possible to determine if those infants given the diagnosis of minimal cerebral damage are the ones who present behavioral and learning disorders.

In regard to this point it is interesting to comment on the judgment made of the mothers. In this group of infants the tension of the mothers increases as the severity of the neurological diagnosis increases. Since behavior problems in children are often attributed to tension in their mothers, the present data raise the question of whether some serious consideration should be given to the other side of the coin, namely, that the infant with difficulties produces the tension in his mother.

Clinicians have long been aware that evidence of early neurological abnormalities can be obtained by history. These clinical hunches are supported by the present findings which highlight some of the signs to be looked for. Even if a detailed developmental examination cannot be done by every physician, a careful and detailed history can be taken. Information about the early behavioral and developmental findings might well lead to the prompter identification of those infants who will later develop disorders, should the hypothesis of the role of minimal cerebral damage in producing them be borne out with time. This history, it should be obvious from the nature of the questions asked, must be taken by the physician, and this task cannot be relegated to the social worker or the psychologist.

The objectivity of the method of examination is indicated by the correlation of the clinical neurological category with the increase in number of abnormalities described. Although a great deal about the natural development of neurological patterns was learned in follow-up study of the 300 infants examined at 40 weeks and at 3 years, further refinement of the procedure is indicated so that clinical acumen can be increased. If a scoring system can be developed the scores on individual items will need to be weighted so that an item which clearly differentiates, such as athetosis, is not given the same weight as an item such as fisted hands. The system will then need to be validated with another group of infants and the findings of more than one examiner compared in a systematic fashion. We are in the process of doing this at

It is clear, however, that a score can never replace clinical judgment. One of the important factors in this judgment is the early behavioral and developmental history. Greater emphasis will need to be placed on this when an attempt is made to evaluate the nature of a neuropsychiatric disability at any age.

Summary

Examination by means of the neuropsychiatric developmental examination of Gesell and Amatruda of 500 premature and 492 full-term control infants

at 40 weeks of age indicates that the amount of neurological damage increases as the birth weight of the infant decreases. Reports of behavior in the first month and up to the time of the examination showed a correlation between the degree of abnormality diagnosed at the examination and certain historical material obtained from the mother. Analysis of 46 individual neurological patterns demonstrated a correlation between the amount of abnormality recorded and the clinical diagnosis of the neurological status and delineated those patterns most useful in discriminating between normal and damaged infants. Particular emphasis is placed on those symptoms which comprise the syndrome of minimal cerebral damage, which was found in 100 infants. The findings emphasize the responsibility of the physician in taking a careful history of early behavior and development in order to evaluate the nature of a neuropsychiatric disability at any age.

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FULMINATING MENINGOCOCCEMIA (WATERHOUSE-FRIDERICHSEN SYNDROME)

REPORT OF TWO PATIENTS SUCCESSFULLY TREATED WITH CHEMOTHERAPY, VASOPRESSORS, AND ADRENAL STEROIDS

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Weight of clinical evidence at the present time favors the combined use of appropriate chemotherapy, vasopressors, and intravenously given adrenal steroids in all cases of fulminating meningococcemia. Reports appear to indicate that there is increased peripheral utilization of steroids in these patients. Review of the literature reveals no consistent picture so far as adrenal hemorrhage is concerned. Combined use of sulfisoxazole or sulfadiazine and intravenously given arterenol and hydrocortisone represents the therapy of choice.

Fulminating meningococcemia (Waterhouse-Friderichsen syndrome) is an overwhelming infection with severe prostration, purpuric or ecchymotic lesions of the skin, and marked hypotension. It is a grave illness carrying a high mortality. The purpose of this paper is to report the cases of two adult patients with fulminating meningococcemia who were treated successfully and to review briefly certain aspects of the therapeutic approach to this disease.

Report of Cases

CASE 1.—A 59-year-old woman was admitted to the Michael Reese Hospital in a semicomatose state on Jan. 31, 1958, at 12:45 a. m. She had returned from India one week prior to admission,

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From the Department of Medicine, Michael Reese Hospital.

apparently in good health. Three days after her return she noted malaise and a vague general discomfort. The next day she developed headache, chills, and fever with temperature of 103.2 F (39.6 C). She was seen by a physician, who prescribed aspirin. The fever persisted throughout the next day, and then the temperature dropped to subnormal levels. Simultaneously she began to lose control of her faculties. Emesis occurred, and a rash appeared over her entire body. She was seen at home by one of us and was noted to be in shock, unresponsive, and gravely ill. Cortisone, 50 mg., was administered intramuscularly, and she was sent to the hospital. Examination on admission revealed the temperature to be 96.6 F (35.9 C) rectally. The blood pressure was 80/0 mm. Hg and the pulse rate 80 beats per minute. The skin was cold and moist and covered with a purpuric and ecchymotic rash. The neck was rigid. The lung fields were clear. Heart examination gave negative findings except for a soft, grade-1, systolic murmur at the apex. Abdominal examination gave negative findings. Painful stimulation elicited only slight withdrawal response. No focal neurological signs were evident.

Lumbar puncture on admission revealed a cloudy spinal fluid with many polymorphonuclear leukocytes and gram-negative diplococci which were typical of meningococci. The spinal fluid glucose level was 6 mg.%. The spinal fluid protein level was 651 mg.% and the chloride level 585 mg.%. The hemoglobin level was 13.1 Gm.% and the white blood cell count 12,150 per cubic millimeter with a marked shift to the left. The blood urea nitrogen level was 54 mg.%, creatinine level 3.4 mg.%, serum chloride level 90 mEq. per liter, serum sodium level 132 mEq. per liter, serum potassium level 3.1 mEq. per liter, and carbon dioxide–combining power 23.4 mEq. per liter. The prothrombin time was 19.2 seconds. A platelet count showed 319,000 per cubic millimeter. The bleeding time (Duke method) was two minutes; the clotting time (Lee-White method) was 16 minutes. A chest roentgenogram was interpreted as being within normal limits. An electrocardiogram showed nonspecific T-wave flattening in all the limb and precordial leads.

Antimicrobial therapy with sulfisoxazole (Gantrisin), penicillin, and chloramphenicol was begun. Intravenously given fluids containing hydrocortisone and arterenol were administered, the latter in a concentration of one ampul (4 mg.) per 1,000 cc. of fluid, at a rate of 40 to 60 drops per minute. The systolic blood pressure was maintained between 120 and 130 mm. Hg. In the first 24 hours she received 8 Gm. of sulfisoxazole intramuscularly, 0.5 Gm. of chloramphenicol intravenously and 2 Gm. intramuscularly, and 2,000,000 units of procaine penicillin G intramuscularly. At the end of the first 24 hours of hospitalization she was more responsive and complained of headache. The blood sulfonamide level was 16 mg.% and was maintained between 10 and 15 mg.% during the remainder of sulfisoxazole therapy.

Arterenol therapy was discontinued on Feb. 3, the blood pressure remaining stable thereafter. The urinary output was adequate, being over 3,000 cc. per 24 hours, and the blood urea nitrogen level decreased to 23 mg.%. The patient became alert, responsive, and well oriented. There were no abnormal neurological findings. On the same day, chloramphenicol therapy was discontinued and the patient was maintained on a regimen of sulfisoxazole given intravenously and penicillin and hydrocortisone given intramuscularly. Sulfisoxazole was given orally in doses of 6 Gm. per day from Feb. 5 to Feb. 22, when this therapy was discontinued. Methylprednisolone (Medrol) therapy was begun in doses of 40 mg. per day on Feb. 5, and the dosage of hydrocortisone was gradually decreased. The remainder of her hospital course was uneventful except for a Monilia infection of the mouth which responded to treatment with nystatin. The dosage of methylprednisolone was gradually decreased to 6 mg. per day at the time of discharge. The skin lesions, many of which had progressed to necrosis, gradually healed. The patient was discharged on March 1, 1958, at which time she had generalized weakness and numbness over the ulnar nerve distribution of the right hand with a diminution in pain perception in this area. The urinary output of 17-ketosteroids was 3.8 mg. per 24 hours.

Case 2.—A 40-year-old man was admitted to the Michael Reese Hospital on June 1, 1954. He had been brought back to Chicago from a fishing trip because of shaking chills, cough, fever, generalized aching, and malaise of 24 hours' duration. On admission he appeared acutely ill, with a temperature of 105.4 F (40.8 C), blood pressure 100/70 mm. Hg, and respiration rate 40 per minute. The skin was flushed, and numerous petechiae were present over the back, arms, and abdomen. A few petechiae were also noted on the conjunctivae and soft palate. There was slight dulness with bronchial breathing and diffuse crepitant rales over the right upper lung field. Neither nuchal rigidity nor focal neurological signs were evident. Shortly after admission the blood pressure dropped to 70/40 mm. Hg.

Lumbar puncture was performed on the day of admission and revealed a pressure of 160 mm. H_2O, Pandy's test reaction 2+, and 13 polymorphonuclear leukocytes per cubic millimeter. The spinal fluid glucose level was 55 mg.%, protein level 38 mg.%, and chloride level 765 mg.%. A second lumbar puncture on June 2 revealed a cloudy fluid and a white blood cell count of 2,380 cells per cubic millimeter, with 92% polymorphonuclear cells. Pandy's test reaction was 4+, the glucose level 97 mg.%, protein level 144 mg.%, and chloride level 709 mg.%. The hemoglobin level was 15.7 Gm.% and the white blood cell count 42,600 per cubic millimeter. The blood urea nitrogen level was 20 mg.%, creatinine level 1.3 mg.%, blood sugar level 191 mg.%, chloride level 117 mEq. per liter, sodium level 141.9 mEq. per liter, potassium level 3.2 mEq. per liter, and carbon dioxide–combining power 17.9 mEq. per liter. There were 300,000 platelets per cubic millimeter. The prothrombin time was 17 seconds, bleeding time (Duke method) two minutes, and clotting time (Lee-White method) 12.5 minutes. Cultures of the blood and of the nasopharynx grew meningococci, type 2. Cultures of the spinal fluid and of the urine were sterile. Viral and rickettsial agglutinations gave negative results. A chest x-ray revealed a left upper lobe pneumonitis and pleural or pulmonary fibrosis in the right upper lobe compatible with old tuberculosis infection. An electrocardiogram showed first-degree atrioventricular block.

On admission the patient was given 1,200,000 units of procaine penicillin G intramuscularly, 5 Gm. of sulfadiazine intravenously, 200 mg. of cortisone intramuscularly, 100 mg. of hydrocortisone intravenously, and oxygen. In addition, arterenol in a concentration of six ampuls (24 mg.) per 1,000 cc. of fluid was administered intravenously at a rate of 20 to 30 drops per minute to maintain the systolic blood pressure between 105 and 110 mm. Hg. The next day the temperature fell to 100 F (37.7 C). On this day auricular fibrillation developed and the patient was rapidly digitalized. Two days later, on June 4, the rhythm reverted to a sinus mechanism. Transient nuchal rigidity and microscopic hematuria were noted at this time. Because of the hematuria, sulfadiazine therapy was discontinued and tetracycline, in a dosage of 400 mg. daily given intramuscularly, was substituted. Because of the history of tuberculosis, the abnormal chest x-ray, and the administration of corticosteroids, antituberculosis therapy with isoniazid, 300 mg. per day, and streptomycin, 1 Gm. given intramuscularly twice weekly, was instituted on June 4. Arterenol therapy was discontinued on June 6, after which the systolic blood pressure remained at a level of 90 to 100 mm. Hg. The dosage of cortisone was gradually decreased from 200 mg. per day, and on June 8 this therapy was discontinued. The further hospital course was uneventful, and the patient was discharged on June 15, 1954.

Comment

In a review of 16 cases, including autopsies, of patients with fulminat[illegible] Ferguson and Chapman[1] [illegible]ad no gross evidence of adrenal hemorrhage. Three other patients showed only slight to moderate adrenal hemorrhage. They concluded that there are no clinical signs by which one can distinguish between patients with and those without adrenal hemorrhage. They observed no correlation between the extent of adrenal damage and the degree of clinical vascular collapse. This inability to determine on clinical grounds whether adrenal hemorrhage has occurred was also noted by Daniels.[2] In a review of 300 cases, with autopsy, of meningococcemia, there were five patients with hemorrhagic adrenals who did not exhibit the clinical picture of fulminating meningococcemia. There were four patients with the classic form of this disease without adrenal hemorrhage.

In 1944 Rich[3] reported that acute infections with the clinical picture of circulatory collapse may produce a necrosis of isolated cells of the adrenal cortex with the transformation of solid cords in the zona fasciculata to tubular structures. He observed these changes in meningococcic, pneumococcic, streptococcic, and diphtheritic infections in patients with the clinical picture of vascular collapse. He stated that most adults with overwhelming meningococcemia, in contrast to children, failed to show a significant degree of adrenal hemorrhage.

Nelson and Goldstein[4] utilized the microscopic findings of Rich to explain those cases of clinical fulminating meningococcemia in which gross adrenal hemorrhage is not seen at autopsy. They postulated that with the same clinical picture the pathological changes in the adrenal glands may vary from microscopic changes in the cortex to complete destruction by hemorrhage.

There remains some difference of opinion regarding therapy in fulminating meningococcemia. The efficacy of antimicrobials is unquestioned. The excellent results achieved with sulfisoxazole[5] and sulfadiazine[6] in the treatment of meningococcic meningitis make these the drugs of choice. This unanimity of opinion is lacking when adjunct therapy is considered. In 1951, Nelson and Goldstein[4] reported two patients successfully treated with cortisone. Tobin,[7] in a report of 63 cases of meningococcic meningitis, encountered nine patients with fulminating meningococcemia. He felt that the effects of cortisone were not spectacular and that, while continuous intravenous infusion of arterenol usually raised the blood pressure, it did not necessarily sustain it. Uhl,[8] on the other hand, reported recovery in a patient with fulminating meningococcemia in whom arterenol was used to treat shock after adrenal cortical extract had failed. Cassidy[9] reported the cases of 17 patients with meningococcic infection, 10 of whom had meningococcemia. In this series, hydrocortisone was administered intravenously in a dosage of 300 mg. per 24 hours, and no case of peripheral vascular collapse developed. Kanter and co-workers[10] noted a mortality of 50% in 10 patients with acute meningococcemia and vascular collapse. They used arterenol, hydrocortisone given intravenously, and cortisone given intramuscularly. Koch and Carson,[11] in a study of a group of infants and children, reported universally poor results, with no difference in the outcome in patients with fulminating meningococcemia between those treated with corticosteroids and vasopressors as compared with those treated before these agents were available.

Kass and Finland[12] determined the circulating blood hydroxycorticosteroid levels in 12 patients with collapse attributable to sepsis of varying etiology. These levels were usually above the normal range, and in none were they below normal. They observed three cases of fulminating meningococcemia in which treatment with sulfonamides and arterenol alone was successful and concluded that there is little rationale for the use of adrenal steroids.

Spink[13] confirmed the work of Kass and Finland by finding normal or increased blood levels of hydrocortisone in patients with severe infection. He also found the plasma half-life of administered hydrocortisone to be significantly less in patients with vascular collapse who eventually recovered than in normal control subjects. The half-life was prolonged in those who did not survive. These reports may be interpreted to indicate that in these conditions there is an increase in the peripheral utilization of steroids until a point is reached in the severity of the illness beyond which the peripheral response fails. Previous studies from this institution have shown that adrenal cortical hormones condition the vascular response to arterenol under certain experimental conditions.[14]

Although the reports are contradictory, we believe the weight of evidence at the present time favors the combined use of appropriate chemotherapy, vasopressors, and intravenously given adrenal steroids in all cases of fulminating meningococcemia. We base this conclusion on the continuing reports of probable clinical efficacy, the suggestion of greater peripheral utilization of corticosteroids in severe stress states, and the experimental work indicating the importance of adrenal hormones in conditioning small blood vessels to vasoconstrictor agents and in preventing capillary disruption.

Summary

Two adult patients were successfully treated for fulminating meningococcemia (Waterhouse-Friderichsen syndrome). The combined use of sulfisoxazole or sulfadiazine and intravenously given arterenol and hydrocortisone represents the therapy of choice.

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SEXUAL POTENCY IN AGING MALES

I. FREQUENCY OF COITUS AMONG CLINIC PATIENTS

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Questions about sexual activity were interspersed among other clinical questions in the examination of 101 men between 55 and 86 years of age. All were ambulant patients whose presenting complaints did not per se constitute impediments to sexual activity. Of 51 patients 69 years or less of age, 33 (65%) were potent in the sense of having copulated at least once in the previous year. Of 50 men over 70 years of age, 17 (34%) were potent. There was a general decline with age, but individual differences were marked, and two of the five men who were over 80 years old stated that they were still active, with 10 as the average number of copulations per year. These results are of fundamental importance in assessing the functional results of various types of prostatectomy.

No adequate survey of sexual activity among aging men is available. Therefore, any surmise about the impairment or decline of sexual function after prostatic surgery or comparable insult to the genitourinary apparatus is necessarily ambiguous. Manifestly, a base line or standard for comparison of sexual activity in men for the decades above 50 years of age is desirable. The present survey represents an attempt to acquire such information.

Since physicians and patients often misinterpret the term "sexual potency,"[1] consensus as to definition is desirable. For purposes of the present report, sexual potency is regarded as the ability to activate psychic ("emotional") desire for sexual intercourse into penile erection adequate for coitus and to achieve gratification (usually ejaculation) during the sexual act. Implicit in this definition is that more than penile erection per se is involved. Moreover, incomplete penile erection with postcoital gratification of wife and/or husband does satisfy the conditions of this definition. Frequency of sexual activity is not important; participation only once annually must be regarded as evidence of potency.

Little information can be found in the literature regarding sexual potency or frequency of coitus in older men. Kinsey and co-workers[2] made brief reference to "old age and impotence," but they attempted no exhaustive survey of this group of men. Dahlen and Goodwin[1a] touched on the subject of loss of potency after open perineal prostatic biopsy; however, some phases of their report have been challenged as equivocal.[3] Young and Davis[4] cited, in general terms, data about sexual performance in patients subjected to perineal prostatectomy. Loss of potency postoperatively was regarded as infrequent, since many of their patients were reportedly in sexual decline before operation. However, present-day opinions—although unverified—regard perineal prostatectomy as the most likely of all such surgical approaches to result in sexual impotency.[5] It is difficult to believe in the objectivity of the data in some reports; others, which fail to cite series of cases, are likewise equivocal.[6]

Neurophysiological integrity was assumed in the present investigation, since it was not our purpose to study this obvious basis for impotency.[7] Our essential interest, admittedly not exploited exhaustively, pertained to the psychophysiological, sociological (mores of the group, occupational stratum, and availability of partner at given time, place, and circumstance), and personal perspectives of the patients. We did not study any specific group of patients, as did Rubin and Babbott.[8]

Material and Methods

Patients were interviewed in the medical and surgical outpatient clinics of the University of California School of Medicine as they waited to see the doctor who would evaluate the particular problems for which they sought advice. In the beginning of our study the "potency survey" was done by fourth-year medical students during the course of taking a full clinical history of each patient. This resulted in many cursory and indifferent reports. The data obtained by the medical students were therefore discarded. This experience also caused us to devise a questionnaire more specific than that originally employed; this questionnaire was used in all subsequent interviews with unselected patients, providing the information for the present report. Questions about sexual performance were interposed among the usual clinical inquiries rather than kept separate, which might have disturbed the patient.

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All patients were in the age range between 55 and 86 years. In no instance was a genitourinary problem the primary cause for which the patient had solicited medical care, although history of such associated problems was occasionally elicited. No patient was included who presented language or other barriers to reliable replies. Sexual intercourse within the preceding year was considered the minimal requirement for inclusion in the "sexually active" group. It was believed that the answers given by patients were grossly reliable. In the age groups evaluated, and under the circumstances of the interview, little if any motivation existed for falsifying the reply.

TABLE 1.—*Sexually Potent Men*

		Occupational Status			Intercourse, Times per Year					Marital Status			
No. of Patients	Age, Yr.	Unskilled	Skilled	Sales and Clerical	1-6	7-12	13-24	25-52	53-104	Married	Widowed	Divorced	Single
11............	55-59	6	3	2	1	3	2	3	2	8	..	1	2
10............	60-64	5	3	2	1	2	2	4	1	8	..	1	1
12............	65-69	5	5	2	5	3	2	2	..	8	..	3	1
11............	70-74	4	4	3	3	1	2	4	1	10	..	1	..
4............	75-79	1	3	..	3	..	..	1	..	2	2	..	..
2............	80+	2	..	..	1	..	1	..	..	..	2	..	..
Total 50............		23	18	9	14	9	9	14	4	36	4	6	4

Results

One hundred one randomly encountered patients were interviewed for and included in this study. As shown in tables 1 and 2 correlations were made between indulgence in or abstinence from sexual intercourse and such factors as age and occupational and marital status.

No essential differences were discernible between men reached through the medical and surgical outpatient clinics, although most patients (66) were encountered in the medical clinic. Therefore, source of the patient was not specified in our final analysis. In no instance was the presenting complaint sufficiently disabling to cause impediment, per se, to sexual activity. All patients were ambulant.

TABLE 2.—*Sexually Inactive Men*

		Occupational Status			Reason for No Intercourse				Marital Status			
No. of Patients	Age, Yr.	Unskilled	Skilled	Sales and Clerical	No Desire	No Partner	No Erection	Partner Refused	Married	Widowed	Divorced	Single
5......................	55-59	1	3	1	4	..	1	..	1	..	2	2
6......................	60-64	1	4	1	3	1	2	..	3	1	1	1
7......................	65-69	4	1	2	6	1	..	..	..	3	2	2
17......................	70-74	6	9	2	15	1	..	1	8	2	1	6
13......................	75-79	8	3	2	13	..	..	..	2	2	1	8
3......................	80+	3	..	..	3	..	..	..	2	1	..	..
Total 51......................		23	20	8	44	3	3	1	16	9	7	19

Of 101 patients about twice as many of the subjects interviewed between the ages of 55 and 69 years were sexually active (33) as were inactive (18). Conversely, the men over 70 years of age were more often inactive (33) than potent (17).

Of the sexually inactive men about one-third were single (never married), a similar number were either widowed or divorced, and one-third were married. Of the entire group 87% gave "no desire" as their main reason for quiescence. Some were included within the category of "no desire" even if they offered a minor or accessory "reason" such as fear of aggravating an inguinal hernia. Some men had penile erections but no desire for coitus; some had no penile erections and also "no desire for sex." We made no attempt to differentiate which situation was primary, i. e., "no desire" or "no penile erection." As cause for sexual inactivity among the remaining 13% (seven patients) who did not copulate, three specified absence of penile erection, three inability to find a coital partner, and one his wife's refusal. It so happened that all single men over 70 years of age were sexually inactive at the time of the interview; some had never had sexual intercourse. Of nine single men under 70 years of age, four were sexually active.

Table 3 summarizes the percentages of sexually active men within different age groups and frequency of coitus within those age ranges. Within our survey occupational status had no apparent bearing on sexual activity or decline. Both laborers and skilled workers, encountered in similar numbers, participated as frequently or were sexually dormant to a comparable degree. Although few "white collar workers" and no professional persons are included in this survey, these data do offer a certain uniformity as to vocational background.

Results to be reported later will include larger proportions of clerical and professional personnel.

Excluded from the present report, although interviewed during our random survey in the medical and surgical outpatient clinics, were eight patients who had had prostatectomy. Five of these were potent, irrespective of age or years elapsed since prostatectomy. The other three patients had not engaged in sexual activity prior to the surgical operation. It was interesting that, despite removal of the prostate as a historical event for a given patient, the operation had no noticeable effect on sexual performance when no current threat was directed against his present sexual potency.

Comment

Age is an indisputable factor relating to decline in the frequency of sexual intercourse. It is not an invariable agent, however, as emphasized by Stokes,[9] since some elderly men averred remarkable sexual aggressiveness. In general, men older than 65 years demonstrate progressively lowered interest and participation in sexual activity.

Table 3.—*Sexual Activity Related to Advancing Age*

Age, Yr.	No. of Patients	Sexually Active, %*	Intercourse, No. of Times per Year†
55-59	16	69	29
60-64	16	63	28
65-69	19	63	12
70-74	28	39	25
75-79	17	24	11
80+	5	40	10
Total	101	49.5	

* These percentages err toward conservatism in excluding men who desired coitus but had no partner.

† Average for group.

It is often presumed that men engaged in "physical" occupations indulge in sexual activity more frequently than those in "sedentary" or "clerical" occupations. Our data do not support this presumption; individual variations are so great as to preclude generalizations.

Collections and analyses of data, such as those by Kinsey and co-workers,[2] are sorely needed. Pure objectivity on the part of subject and interviewer may not be realized but should be pursued. Errors on the part of the patient as well as the interviewer are inevitable. For example, as Dahlen and Goodwin[1a] noted in their report, "it was not always possible postoperatively to be certain of the patient's memory of his potency prior to operation."

This survey was considered too limited for drawing conclusions concerning national origin, race, religion, or financial status. Such factors as the leisure time available to retired people and the mores of a given community were not evaluated at this time, although these doubtlessly affect a person's sexual interests.[10] By the same token, we did not analyze any patterns of sexual frequency established in younger years in relation to the patient's sexual interest and behavior in later life. In speculative terms, however, it would seem unlikely that a man of conservative sexual interests in his early adult life would suddenly blossom forth as a satyr in his older years. In similar terms, we did not pursue the matter of whether the wife's company all day would dull sexual ardor in older men retired from active employment. Finally, it appeared that moral self-determination is flexible, i. e., human frailty is such that many men transgress the bounds of propriety and become sexually potent with extramarital opportunities while remaining inert in their marital environment.

Summary

The sexual activity of 101 men over 55 years of age was recorded by personal interview. Within our definition of sexual potency about twice as many men up to 70 years of age were sexually active as those over that age. Among sexually potent men marital status was more influential than occupation or age in encouraging continued sexual activity.

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PILONIDAL SINUS CARCINOMA

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More thorough gross and microscopic study of pilonidal sinus specimens may reveal a higher incidence of carcinoma than has been indicated in the medical literature. Gross symptoms suggesting malignant change include bleeding, ulceration, and overgrowth. These are especially noteworthy when occurring in sinuses present for many years. Surgery consists of wide and deep excision. Carcinoma in a pilonidal sinus is most commonly of the squamous cell type, slow in growth and not prone to metastasize.

Carcinoma complicating pilonidal sinus is rare. There have been recorded in the surgical literature only 12 cases, 1 of which was published by us in 1957.[1] Within a month after this publication, a second patient with pilonidal carcinoma appeared, an unusual occurrence for one surgical practice. The present article will afford an opportunity not only to present this second case but also to report a follow-up study of the first patient four years after the operation.

Up to the present time the literature documents only 12 cases of pilonidal sinus with superimposed carcinoma. Although chronic irritation and inflammation have always been mentioned and accepted as causes for carcinoma, malignancy in chronic draining sinuses is not considered too common.[2] As far back as 1828, Marjolin[3] reported carcinoma in skin ulcers. In 1833 Hawkins[4] noted carcinomas forming in the scars of fistulas. McAnally and Dockerty[5] of the Mayo Clinic added several cases to the literature in 1949 in a study on the development of malignancy in draining sinuses. However, their patients had the chronic suppurating sinuses of osteomyelitis, empyema, and anal fistula.

A malignant neoplasm in a pilonidal sinus is slow growing and therefore has a good chance of being cured by early radical surgery. Metastases occur late, and the location in the sacrococcygeal region permits a wide excision of the growth. The skin and subcutaneous tissue should be excised at least 2 in. from any recognizable tumor tissue if one hopes to eradicate the disease completely. After this the dissection must advance into the depth of the wound so that the specimen is removed en masse from the fascia of the gluteal muscles laterally and the periosteum of the sacrum and coccyx medially. Hemostasis is easily controlled with the coagulating current, and the wound is packed in the wide open position. In about a month the wound is filled with granulation tissue and is ready for skin grafting.

Our first case of pilonidal sinus carcinoma occurred in a 43-year-old man with a 21-year history of a periodically draining mass in the sacrococcygeal region. At operation on May 27, 1955, with the patient under spinal anesthesia, a radical excision was performed with complete removal of the tumor, sinuses, and a generous surrounding area of normal tissue. The wound was left open and packed with gauze. The patient was readmitted for skin grafting on June 30, 1955. The skin defect was completely covered, the patient remaining in the hospital for eight days, after which he was discharged with a well-healed wound. Pathological diagnosis was squamous cell (epidermoid) carcinoma arising in a pilonidal sinus. This man has been given frequent follow-up examinations and is alive and well without any evidence of recurrent disease for a period of four years.

Matt,[6] in September, 1958, reported the 12th case of pilonidal carcinoma. This was in an 18-year-old male with a one-month history of sanguinopurulent discharge over the region of the sacrum and coccyx. The lesion was totally excised and subsequently diagnosed as a mixed basal and squamous cell carcinoma of a pilonidal sinus tract and perianal skin. A satisfactory six-year follow-up period was reported. Our second case of a pilonidal sinus carcinoma is herewith reported, making the 13th case to be recorded in the literature.

Report of a Case

A 51-year-old man was first examined on July 30, 1957. He gave a history of having had a discharging sinus over the lower part of the spine for 15 years. This became infected at least two or three times a year and drained spontaneously. He first noticed bleeding in July, 1957. His general health had always been good with no serious medical or surgical illnesses. The family history was noncontributory.

Physical examination revealed a healthy, obese man weighing 186 lb. (84.4 kg.). His blood pressure was 140 mm. Hg systolic and 90 mm. Hg diastolic. The rest of the examination gave essentially negative results except for the local findings. In the sacrococcygeal region, 4 in. above the anus and extending to the right of the midline, there was an area 6 cm. in diameter with seven or eight discharging sinuses and cicatrized tracts. The lymph nodes in the right groin were slightly enlarged and firm but mobile. There were no enlarged nodes in the axillae or left groin.

On Aug. 7, 1957, a radical extirpation of the lesion was performed. The entire mass was widely excised down to the gluteal fascia and the periosteum of the sacrum and coccyx. The wound was left open and packed with gauze.

The surgical pathological report showed the specimen to consist of a roughly oval mass of skin and subcutaneous fat, measuring 130 mm. in one diameter and 115 mm. in the other and averaging approximately 40 mm. in thickness. Arising from the center was a raised, granular, somewhat papillary mass which protruded about 15 mm. above the remainder of the skin surface. The mass varied in color from a light gray to a dirty brown and had ulcerated areas. The cut surface was light gray and friable. Microscopic examination showed living stratified squamous epithelium, most of which had been replaced by atypical squamous cells. These extended irregularly into the subcutaneous tissue. Pearl formation was prominent; focal lymphocytic and plasmacytic infiltration were also present. The pathological diagnosis was squamous cell (epidermoid) carcinoma.

He remained in the hospital four days, and on Sept. 20, 1957, five weeks after discharge, he returned for a skin grafting operation. He was discharged for the second time on Sept. 26, 1957, with a complete "take" of the graft. He was reported doing well until Oct. 4, 1957, eight days after his second hospital discharge, when he suddenly died at home. Death was clinically diagnosed as due to a pulmonary embolus, even though no autopsy was performed.

Comment

A review of the pathology of all of the 13 cases of pilonidal sinus malignancy reported thus far reveals the presence of variegated forms of carcinoma. A summary of the reported cases is given in the table.

Almost all the patients had symptoms which should have been considered possibly serious if they occurred in old pilonidal sinus wounds: (1) long-standing and persistent sinuses with drainage, (2) sudden, rapid growth, (3) overgrowth, above the skin level, (4) friability, (5) ulceration, (6) hemorrhage into the tissues, and (7) external bleeding. The most common observation related by the patients was bleeding that occurred in sinuses present for many years.

Summary

Malignant neoplasms are found implanted in pilonidal sinuses infrequently. This is not consistent with the accepted theories as to the relation of cancer to chronic inflammation. In the literature in which the type of carcinoma was mentioned, squamous cell (epidermoid) carcinoma was the most common type of malignant pathology, occurring in 7 of 11 patients. Two cases remain unclassified as to the type of carcinoma.

Bleeding, ulceration, and overgrowth are symptoms which may be suggestive of malignancy. Carcinoma in a pilonidal sinus is slow in growing and not prone to metastasize early. The surgical procedure consists of a wide excision extending 2 in. away from all pathological tissue and proceeding deeply down to the periosteum of the sacrum and coccyx and the gluteal fascia.

Types of Carcinoma in Pilonidal Sinuses as Reported in the Literature

Author	Squamous Cell	Basal Cell	Mixed Basal and Squamous	Adenocarcinoma	Unclassified
Wolff, H.: Arch. klin. Chir. 62:731, 1900	1				
Singleton, A. O., Sr.: Tr. South. S. A. 50:71, 1937					1
Nosti, R.: An. cir. 3:261, 1937	1				
Schubert, H.: Zentralbl. Chir. 66:2008, 1939	1				
Goldmann, H., and Kalow, I.: Bull. Hosp. Joint Dis. 4:89, 1940		1			
Tendler, M. J.: South. M. J. 34:1156, 1941				1	
Baraldi, A.: Bol. Soc. cir. Rosario 9:103, 1942					1
Vara-Lopez, R.: Rev. clin. españ. 24:367, 1947	1				
Hall, A., and Lee, J. G.: Cancer 9:760, 1956	1				
Hayden, E. P.: New England J. Med. 255:854, 1956			1		
Weinstein and others [1]	1				
Matt [6]			1		
Present study	1				
Total	7	1	2	1	2

A more thorough gross and microscopic examination of pilonidal sinus specimens may reveal more carcinomas. A 13th case of pilonidal sinus carcinoma is herewith added to the surgical literature, the second case to be reported by us.

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FOLLOW-UP STUDY ON A GROUP OF OLDER AMPUTEE PATIENTS

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Detailed interviews were held with 51 amputees followed for varying periods after fitting of prostheses and release from hospital. Psychological factors affecting attitude and motivation seemed to be operating to various degrees. Favorable morale regarding value and use of the prosthesis by individuals appeared to be related to degree of change in physical condition, mode of living, and restriction on activities. It is believed worthwhile to provide prostheses with assistive devices for older amputees in order to help them remain more functional in their self-care, ambulation, and posthospital adjustment.

With the increasing number of older patients in the hospital population, it is pertinent to study various aspects of treatment and the outcome as it relates to such individuals. The purpose of this study was to obtain follow-up data concerning the posthospital adjustment of a group of older patients for whom the amputation of a limb or limbs had been necessary. The major areas investigated were physical status, mortality trends, personal and socioeconomic adjustment, and the extent to which a prosthetic appliance had been prescribed and was actually being used.

Patients included in this study were 55 years of age or older at the time of surgery and had been out of the hospital at least one year by the time of the follow-up interview. Through the assistance of the medical record librarian, cases were identified and initial data entered on work sheets for amputee patients who were in the designated age range and who had been discharged from this 712-bed general medical and surgical hospital, the Veterans Administration Hospital, Oakland, Calif., between Jan. 1, 1950, and April 30, 1955. There were 53 such patients. We were able to obtain follow-up information on 51 men, who comprised the number in this study.

The method of investigation consisted of two parts: a review of the hospital records and a follow-up survey. Clinical, physical medicine and rehabilitation, and social work service records were examined concerning pertinent areas which were uniformly reported. A schedule was prepared and a follow-up survey was carried out through social work service. An essential part of this was a personal interview with each ex-patient as a means of making observations and of getting first-hand information.

Hospitalization Data

Background Information.—All 51 amputees were males. Sixteen patients were between the ages of 55 and 59.9 years, 22 between 60 and 64.9, and 13 over 65 (one man was 82). The mean age was 63.1; the median age was 62.0 years. Three-fourths of these patients were under 65 years of age. Information concerning marital status and mode of living prior to admission to the hospital is combined in *table* 1.

One-half of the patients were married. All but two of these had been living at home. One had been at a state veterans home; the other, who had been in a Veterans Administration domiciliary, became ill when on holiday leave to visit relatives and was admitted to the hospital. Twenty-five patients were single, divorced, or widowed, and for them there was a diversified pattern in mode of living. Fifteen had lived by themselves in an apartment, room, hotel, or cabin; five had been residing with a relative; four were transferred for hospital treatment from a state veterans home; and one was transferred from another hospital after a cardiovascular accident.

Ten of these 51 patients who were under the age of 65 were reported to have been employed prior to admission. Of those patients over that age, none was reported to have worked for some time. This employment picture appeared to be related primarily to conditions in the labor market affecting older workers and to the high incidence in this group of chronic illness which imposed limitations on occupational activity.

Major Pathological Condition and Reason for Amputation.—A characteristic of this group was the prevalence of multiple diagnoses. The major pathological condition was arteriosclerotic cardiovascular disease in 23, general arteriosclerosis in 10, diabetes mellitus with arteriosclerosis obliterans in 5, embolism and/or thrombosis in 5, traumatic fracture in 2, chronic osteomyelitis in 2, carcinoma in 2, thromboangiitis obliterans in 1, and traumatic arthritis in 1. The predominant major illness was arteriosclerotic cardiovascular disease, which occurred in 45.1% of the total number of patients. Those with some type of major arteriosclerotic involvement

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numbered 38 (74.5%) of the patients studied.

A trend in connection with age appeared when compared with diagnostic groupings. Of the 38 patients suffering from a major arteriosclerotic involvement, 78.9% were 60 years of age or older. For the 13 having other major pathological conditions, 61.5% were under 60.

By far the most frequent complication which was the reason for performing an amputation was that of gangrene. This occurred in 37, or 72.5%, of the cases. There were four instances of osteomyelitis; three each of ulcer and embolism; and one each of vascular insufficiency, nonunion old fracture, purulent drainage, and epidermoid carcinoma.

Fifteen patients had sympathetic blocks, 4 of them having had more than one block; 17 patients had sympathectomies, of whom 5 had bilateral sympathectomies. Six of the above 32 had both a sympathetic block and a sympathectomy. In spite of these therapeutic surgical interventions to improve circulation, it was still necessary to perform an amputation at a later date on all of these patients.

TABLE 1.—*Marital Status and Mode of Living of Patients Prior to Admission to VA Hospital*

	Patients					
Mode of Living	No	%	Married	Single	Divorced	Widowed
With own family......	24	47.1	24	..	..	..
By self................	15	29.4	..	9	4	2
Domiciliary setting....	6	11.8	2	..	3	1
With relative..........	5	9.8	..	3	1	1
Other hospital.........	1	1.9	..	..	..	1
Total................	51	100.0	26	12	8	5

Site of Amputation.—The site of amputation was above the right knee in 24, above the left knee in 14, bilateral in 10, upper part of the left arm in 2, and below the left knee in 1. There was a preponderance of amputations above the knee on the right side. It was thought that one factor affecting this might be poor sitting posture, namely, with the leg on the dominant side being crossed more often.

Of the 10 bilateral amputees, 9 had a major arteriosclerotic involvement. Two had double above-knee amputations while hospitalized, and eight had had previous amputations. For these eight, the time intervening between the two surgical procedures tended to fall into two patterns; for five the interval was from 12 to 24 months, and for three it was between 56 and 62 months. The resulting situation was that, of the 10 bilateral amputees, 6 had both amputations above the knee and 4 had one above-knee and one below-knee amputation. The high incidence of amputations above the knee, whether unilateral or bilateral, posed a greater problem in terms of rehabilitation and ambulation training.

Deaths in the Hospital.—Four of the 51 patients died in the hospital. All had suffered from arteriosclerotic cardiovascular disease. Their ages were 63, 68, 71, and 78, all being older than the average age for the total group. There were, then, 47 amputee patients who were discharged from the hospital.

Patients Receiving Prosthetic Appliances.—The decision as to whether or not a patient was going to be issued a permanent prosthesis was based primarily on a careful medical appraisal of the nature and extent of the patient's illness or injury in relation to his physical and mental capacity to use a prosthesis and the effect on his functional efficiency in performing activities of daily living outside of the hospital environment.

Such an evaluation required a thorough and comprehensive review of not only all the medical factors involved but also the nonmedical aspects. In this respect, the importance of peripheral vascular tests cannot be overlooked as a base line in evaluating the circulation of the limb or limbs concerned. These tests were significant not only in determining the necessity for amputation but as a follow-up evaluation of the condition of the extremity or extremities under medical and physical therapy treatment.

Of the 47 patients, 26, or 55.3%, were fitted with and trained in the use of prosthetic appliances. This included one arm amputee. For the second arm amputee, the stump was too short for a prosthesis to be feasible. There was variation according to age and major pathological conditions in patients who received prosthetic appliances. Of the patients aged 55 to 59.9 years, 10 received prostheses and 6 did not; of those aged 60 to 64.9, 14 received prostheses and 7 did not; and of those aged 65 and over, 2 received prostheses and 8 did not. Of the 34 patients with a major arteriosclerotic involvement, 15 (44.1%) received prostheses; of the 13 with other major pathological conditions, 11 (84.6%) received prostheses.

Of the 10 bilateral amputees, prostheses were issued to 3. Two were 55 and one was 59 years old. One used a prosthesis which he had, plus crutches. One used an old prosthesis plus a new one and crutches, and the third was issued an above-knee-right and a below-knee-left prosthesis and crutches.

Physical Medicine and Rehabilitation Prosthetic Training Program.—The prosthetic program comprised four phases. Phase 1—bed training—consisted primarily of body positioning, general conditioning, and bedside stump exercises. Phase 2—clinical training—consisted of preambulatory and crutch training, bandaging, and exercises such as mat, general conditioning, and Buerger-Allen exercises. Phase 3—pylon training—consisted of progressive resistive exercises to stump, pylon training, balancing in parallel bars, and continuation of Buerger-Allen exercises, bandaging, and mat exercises as indicated. Phase 4—prosthetic training—consisted of a continuation of all activities of phase 3, when indicated, except that prosthetic training was conducted instead of pylon training. Concurrent with this prosthetic training, the patients participated in an intensive self-care program.

The use of a pylon in ambulation training was one of the most important phases of the amputation program. Generally, about six to eight weeks after surgery a plaster bucket was made of the patient's stump, either above-knee or below-knee. The plaster bucket was then inserted into the leather cuff of the pylon, which could be adjusted to the individual patient's needs.

Pylons have proved advantageous in our program in (*a*) shrinking and seasoning a stump for preparation of a permanent prosthesis; (*b*) retraining of the proprioceptive tracts during the shrinking period, thus enabling the patient to build confidence in balance and coordination while ambulating; and (*c*) eliminating the cost of expensive bucket adjustments which are necessary when preparing a stump during training for a permanent artificial limb.

Social Work Service.—A number of these patients came to the attention of social work service at an early point as the result of personal difficulties connected with hospitalization or impending surgery or because of financial or family difficulties. Because of social, economic, or emotional complications, other patients became known later on. Some requests for a social evaluation, as a part of rehabilitative or treatment planning, were made initially and some at a subsequent point in hospitalization. Despite the specific problem presented, the factors of the threat represented by amputation, the imposition of limitations of activity, and concern about the future were reactions with which the patients needed help. In the process of discharge planning, it was necessary to mobilize to the utmost the capacities existing in the patient and his family, including all relatives, and to utilize all available community resources. With a number of these older patients a problem was to conteract their reluctance to leave the hospital. The general pattern was not so much one of continuous activity with the patient but rather that of giving the needed services according to an integrated timing with on-going treatment and rehabilitative planning.

TABLE 2.—*Period of Hospitalization of Patients*

	Patients, No.	Days Hospitalized, Median No.	Days from Amputation to Discharge, Median No.
With prosthesis	26	192.5	133.0
Without prosthesis	21	120.0	90.0
Total	47	154.0	112.0

Period of Hospitalization.—There was a wide range in the number of days of hospitalization, varying from 52 days to periods of 573 and 579 days for two patients with resistive bone infections. The mean was 147 days, there being four patients with that period of hospitalization. Because of the two atypical cases, the median, rather than the mean, was computed for each group (table 2). For the total group the median number of days hospitalized was 154.0, and the median interval between the date of amputation and the date of hospital discharge was 112.0 days. It is of interest to note that the difference in number of hospital days from amputation to discharge was only 43 days higher among those who had received prostheses than those who had not.

Capacity for Self-care and Ambulation.—At the time of leaving the hospital 32 of the 47, or 68.1%, were completely able to care for their personal needs, while 15 needed partial assistance. Since the capacity to ambulate was not involved for the two arm amputees, the number reviewed here is 45. The categories used were based on the prevalent or customary way of getting around.

Twenty-five leg amputees had been fitted with prostheses. One ambulated with the prosthesis alone, 10 with the prosthesis plus a cane, and 13 with the prosthesis plus crutches. One 71-year-old man, who was insistent that he be given a prosthesis, was able to use it only part of the time with the aid of crutches, but he actually depended on crutches to get about, and was so classified. Six ambulated with crutches alone. Fifteen got about in a wheel chair, seven of them being the bilateral amputees for whom prosthetic appliances were not believed to be advisable. All of these patients were given intensive self-care training so as to be functional in a wheel chair.

Posthospital Living Arrangements.—Of the 47 patients who were discharged, 21 of the 24 married men returned to live with their own family. Six single, three divorced, and one widowed went to live by themselves in an apartment, room, hotel, cabin, or a place where they had room and board. This mode of living had been their pattern in the past and was one which they preferred to try again on leaving the hospital. Of the eight who went to a domiciliary setting or state veterans home (three of whom were married, one single, two divorced, and two widowed), five had been transferred from there, and this was the most feasible discharge plan for an additional three. Of the seven who went to live with relatives (four of whom were single and three divorced), three went to a sister, two to a daughter, one to a son, and one to his wife's mother. One single man was transferred to a county hospital for care of chronic conditions.

When the mode of living prior to admission was compared with that at the time of discharge, it was found that the percentage of those in their own home remained about the same. There was a drop in the number of those living by themselves and an increase for those going to a domiciliary setting or to live with a relative.

Follow-up Data and Survey

Mortality Data.—On completion of the follow-up survey, it was found that, of the 47 patients who had been discharged from the hospital, 15 had died. These, added to the 4 who had died in the hospital, totaled 19, or 37.3%, of the original 51 patients in the study.

Table 3.—*Major Pathological Condition of Patients Who Died*

Major Diagnosis	Total	Died No.	Died %
Diabetes mellitus with arteriosclerosis obliterans	5	3	60.0
Arteriosclerotic cardiovascular disease	23	12	52.2
General arteriosclerosis	10	2	20.0
Embolism and/or thrombosis	5	1	20.0
All other	8	1	12.5
Total	51	19	37.3

Of the 15 who died after having been discharged, 9 had been readmitted to this hospital for a total of 21 times, usually for treatment of the same conditions or for complications connected with them. In four instances a stump revision was necessary. For one patient with general arteriosclerosis the amputation of the other leg had to be done within six months. Some of the patients died in this hospital, but a number did not; therefore, we do not have uniform data as to the specific cause of death.

A correlation between major pathological condition and mortality trend appears in table 3. The mortality trend was considerably greater for those in whom arteriosclerotic involvement was complicated by a diabetic or a cardiovascular condition. It was the same for those having general arteriosclerosis and those with embolism and/or thrombosis and was much less for those with other diagnoses.

The mortality trend according to unilateral and bilateral amputees and in regard to those having and those not having prostheses is given in table 4. The intervening time for the total number who died after leaving the hospital ranged from 14 to 45 months, with an average of 27.9 months, or well over two years. The average for the bilateral amputees was slightly higher than for those with one leg amputated.

Of the total, four had prostheses when they left the hospital. Subsequently one unilateral and one bilateral amputee had been fitted with a prosthesis. For another patient, the amputation of the remaining leg had been necessary and an additional prosthetic appliance had been prescribed. Thus, the total having prostheses became six; these lived from 24 to 45 months, or an average of over three years. The nine who had no prostheses lived from 14 to 35 months, with an average of less than two years.

As to age, the average time out of the hospital for the 15 amputees who later died was 32.0 months for six in the 55-to-59.9-year age group, 28.2 months for the five in the 60-to-64.9-year age group, and 21.5 months for the four who were 65 years of age or older.

Method of Survey.—Of the patients discharged, 32, or 68.1%, were interviewed by a social worker at their place of residence. In this way the items in the survey schedule were covered and an opportunity was provided for direct observation. These contacts were usually made without prior notification to the ex-patient. Twenty who lived within the geographical area around the hospital were seen by one of us (D. M. B.). Nine who were living in different parts of the state and three who were in other states were interviewed by social workers from various Veterans Administration regional offices. In nearly all instances, these former patients felt that the visit was an indication of interest in how they were doing and they were quite willing to discuss their situation.

Period Between Hospital Discharge and Follow-up Interview.—One of the criteria for selection of this group was that each patient be out of the hospital at least one year by the time of the follow-up survey in 1956. The actual interval between hospitalization and follow-up ranged from 14 to 72 months, with the frequency distribution being fairly even. The mean was 39.4 months and the median 36.0 months.

Physical Status.—Considering the age of these amputees and the prevalence of degenerative disorders, it was not surprising that 20 of the 32 had been rehospitalized here or elsewhere. Seven, including three who had been rehospitalized, had received treatment from a private physician, and one had been treated at a county hospital. Of the 20 who were rehospitalized, 9 experienced difficulty with the stump, 5 had a stump revision, 2 reported continuance of phantom pain, and 3 (all of whom had arteriosclerotic cardiovascular disease) required an above-knee amputation of the other leg within 11, 14, and 24 months respectively. Of the total of those in the follow-up survey and those who died after having left the hospital, nine, or 19.1%, had to have a stump revision, and for four, or 8.5%, the amputation of the other leg became necessary.

Table 4.—*Number of Months Between Hospital Discharge and Death of Fifteen Patients*

Site of Amputation	Patients, No.	Mo. Intervening, Av. No.
Unilateral—above knee	9	26.2
With prosthesis	3	33.3
No prosthesis	6	22.7
Bilateral—above knee	6	30.5
With prosthesis	3	42.3
No prosthesis	3	18.7
Total	15	27.9
With prosthesis	6	37.8
No prosthesis	9	21.3

Inasmuch as the individual's feeling about his physical condition played an important part in his general attitude and adjustment, this point was covered with each amputee. Fourteen reported their conditions were good, 13 fair, and 5 poor. These subjective reactions appeared to be related not only to the presence of symptoms or of discomfort and the recency of having received treatment but also to their ability to ambulate or to move about and to their capacity for caring for their personal needs.

It was interesting to note that only four of the amputees were still protesting the loss of a limb. The others had, in varying degrees, and better for the unilateral than the bilateral amputees, come to a psychological acceptance of the loss of their limb or limbs. One man, an obviously poor candidate for a prosthesis, was resentful because he had not been given one. There seemed to be the possibility that his feeling was related to others having been issued prosthetic appliances in the domiciliary where he was living. Three former patients expressed the reaction that their hospitalization had not included sufficient treatment or had not been long enough. On checking the records, however, it was found that considerable effort had been expended in their treatment, that they had all been trained in the use of their prostheses, and that they had all been hospitalized much longer than the average.

Table 5.—*Mode of Living and Marital Status of Amputees at Time of Follow-up*

	Patients					
Mode of Living	No.	%	Married	Single	Divorced	Widowed
With own family......	14	43.8	14	..	..	..
With a relative........	6	18.7	1	3	1	1
By self..................	4	12.5	..	2	2	..
Domiciliary setting....	4	12.5	..	..	2	2
Other hospital.........	4	12.5	2	1	1	..
Total................	32	100.0	17	6	6	3

Ability for Self-care.—The ability for self-care at the time of follow-up compared with that at time of leaving the hospital was as follows: There was a drop in the number of those who were capable of taking care of their own needs (from 24 patients to 19), a slight increase among those requiring partial assistance (from 8 patients to 9), and a definite increase for those needing full-time care (from no patients to 4). Of the four in the last category, one was a bed patient at home, and three were in the hospital unit at a state veterans home.

With age and physical limitations, there appeared to be a decrease in capacity for self-care and an increase in the need for arrangements where more care or supervision could be provided. This observation was reflected also in the material in the next section.

Mode of Living and Marital Status.—Table 5 shows data on the mode of living of the amputees at the time of follow-up. Of the 17 married men, 14 were living with their families, 1 was with a relative, and 2 were hospitalized at a state veterans home. Of the 15 who were either single, divorced, or widowed, 5 were living with a relative, 4 were living independently, 3 were residing at a state veterans home, one was at a Veterans Administration domiciliary, and 2 were hospitalized at a state veterans home.

A comparison of percentages as to the mode of living at the time of admission, at the time of hospital discharge, and subsequently at the time of follow-up revealed the following trends: The number of those living with their own family remained the most constant, with only a small decrease in the percentage; there was a marked drop in the number of those living alone and an increase for those in a domiciliary setting. Twice the number were living with a relative, while there was a noticeable increase in number of those in another hospital.

Only 6 of the 32 amputees had made shifts in living arrangements between the time of hospital discharge and follow-up. Two had merely moved from the home of one relative to that of another. Four had been living alone; of these, two had moved to the home of a relative and one had gone to a Veterans Administration domiciliary and one to a state veterans home. This relative lack of mobility may be partially explained by the age and physical disability of this population. It also indicated that the plan at the time of leaving the hospital, if suitably made, was likely to be the continuing living arrangement for a person in a group such as this.

Vocational and Financial Situation.—One amputee was gainfully employed full time at reconditioning valves in his own shop. Three others were working part time; one did repair work and saw-filing in his workshop at home, one supported himself and his wife by operating a concession in an amusement park, and the third operated a lodge in the hills where he lived during the hunting season. All four men were between 61 and 66 years old, all had an above-knee amputation of the right leg, and all had been fitted with prostheses. They had been out of the hospital for 14, 26, 36, and 62 months respectively. They all expressed the opinion that having a prosthesis was most helpful in enabling them to pursue a vocational activity. Their general attitude was observed to be very good.

Financially, it was found that two men were fully self-supporting. Another received Social Security and Old Age Assistance benefits. The remaining 29 were in receipt of Veterans Administration benefits. For 14 of these, this was their sole source of income. This income for the other 15 was supplemented by Social Security or retirement benefits, by the wife working in five instances, by part-time work for two, and by Old Age Assistance for one. Of the 32 amputees, 6 who were married and 4 of the others reported having a difficult time financially. Twenty-two stated that they were managing adequately.

Recreational Activities.—The recreational activities of this group seemed to be influenced by the individual's capacity to move about, his attitude toward his physical condition, and his living situation. An examination of the changes in recreational patterns was not possible inasmuch as there was little information available regarding recreational activities prior to the amputation. Our observations will be limited to the activities in which these amputees were engaging when they were interviewed for this study.

Recreational activities were classified as active or passive. Active recreation included gardening, walking, hiking, fishing, dancing, bowling, or such creative hobbies as wood carving or metal work. The passive forms of recreation were reading, listening to music, watching television, attending motion pictures, or card playing.

Thirteen amputees engaged in active types of recreation (this, of course, did not exclude passive recreation), while 19 were interested only in passive amusements. Of those who engaged in active recreation, 10 had prostheses and 3 did not. It appeared that a family living situation was more conducive to active recreational activities.

Table 6.—*Mode of Ambulation*

Mode	When Leaving Hospital Total No. of Patients	When Leaving Hospital Unilateral	When Leaving Hospital Bilateral	At Follow-up Total No. of Patients	At Follow-up Unilateral	At Follow-up Bilateral
Prosthesis alone or plus aid	19	17	2	15	14	1
Crutches alone	4	4	..	4	4	..
Wheel chair	7	4	3	9	4	5
Bed patient	..	..	..	2	..	2
Total	30	25	5	30	22	8

Ability to Ambulate or to Move About.—The capacity to ambulate did not affect the two arm amputees; therefore, the number considered in this section will be the 30 leg amputees. At the time they left the hospital there were 24 above-knee, 1 below-knee unilateral, and 5 bilateral amputees. Between that time and the follow-up interview, it had become necessary to remove the other leg for three above-knee amputees, which increased the number of bilateral amputees to eight. In addition, 21 amputees in the follow-up survey had been fitted with prostheses while hospitalized, but afterward two others obtained prostheses, making a total of 23 by the time of follow-up.

Considering the changes mentioned above, comparative data in table 6 regarding typical mode of getting about are based on both that at the time of leaving the hospital and that at the time of follow-up. There were no over-all changes among the unilateral amputees in regard to mode of getting about except for three who had required the amputation of the other leg. Of the eight bilateral amputees, however, only one (who had an above-knee and Symes amputation) was able to ambulate adequately, whereas five were confined to a wheel chair and two had become bed patients.

Next, the mode of moving about was examined more specifically, and the extent of ability to get about was appraised (table 7). At the time of leavin the hospital only one amputee had been able to ambulate with his prosthesis alone. At the time of follow-up this was true for eight, who could go as far as they wished or walk for moderate distances. The seven who ambulated with their prostheses plus a cane or crutches did equally well, except for two who were restricted to moving about their quarters. Of the 13 who got about on crutches or in a wheel chair, 10 moved about their quarters only, and two had become bed patients.

Table 7.—*Ability to Move About*

Mode	Total No. of Patients	As Much as Desired	Moderate Distances	Around Quarters Only	Not at All
Prosthesis alone	8	5	3	..	..
Prosthesis plus cane	4	2	2	..	..
Prosthesis plus crutches	3	1	..	2	..
Crutches alone	5	1	1	3	..
Wheel chair	8	..	1	7	..
Bed patient	2	..	..	..	2
Total	30	9	7	12	2

Extent of Use of Prosthesis.—Of the 32 amputees, 24, or 75%, had received prostheses by the time of the follow-up interview (table 8). This number included one arm amputee who used his prosthesis some each day but who tended to do most things with his uninvolved arm. Thirteen, or 54.2%, were using their prosthetic appliances regularly and consistently, and 3 used theirs some each day, but not as extensively as the 13.

That a certain amount of complications for a group of this age could be anticipated was borne out by their experiences. Nine reported pain, swelling, dermatitis, or other trouble with their stumps; two had a continuation of phantom pain; and five required stump revisions. Twelve, or one-half, reported having mechanical trouble or difficulty with the fit of the prosthesis. Most had had theirs repaired; two had been issued new prostheses.

Table 8.—*Extent of Use of Prosthesis*

Extent	Total No. of Patients	Unilateral Prosthesis	Bilateral Prosthesis
Regularly and consistently	13	12	1
Some each day	3	3	..
Infrequently	2	2	..
Not at all	6	5	1
Total	24	22	2

It appeared, however, that such physical or mechanical complications did not wholly explain the individual's adjustment to and use of the prosthesis. Psychological factors affecting attitude and motivation seemed to be operating to various degrees. Difficulty with stumps or prosthetic appliances did not appear to assume as much significance for those who used theirs consistently as it did for some of the others. For example, the three men who used their prostheses some each day were reported as being bored and inactive, afraid because of several falls, and complaining and seeking sympathy. Of the two who used their appliances only infrequently, one was reported to have "given up." His wife stated that he used his appliance very little because he "was afraid" and "had no nerve." The other man tended to project all blame for his situation outside himself and doubted if he "could do anything about it." This aspect also appeared to be operating with two of the amputees who were not using their prostheses at all.

Of the six men who were not using their prosthetic appliances at all, two, aged 62 and 71, both with arteriosclerotic cardiovascular disease, had within 11 and 14 months had an amputation of the other leg and had been confined to a wheel chair. Two other men, one aged 55 who had arteriosclerotic cardiovascular disease and one aged 59 who had diabetes mellitus with arteriosclerosis obliterans, had had cerebral accidents and were wheel-chair patients.

The remaining two had discarded their prostheses. One, a 60-year-old single man and an alcoholic, was living on skid row and getting about on crutches. The other, a 65-year-old single man who was living with a relative, depended on crutches and had never tried to use his prosthesis. He said that he felt he was "about to die" and that he "did not care anymore."

Thus, it was found that, of the 24 amputees who had prostheses, 16, or 66.6%, used theirs regularly or some each day. Four, or 16.7%, had been forced to discontinue the use of theirs because of another amputation or because of a stroke. Four, or 16.7%, used their prosthetic appliances only infrequently or had discarded them.

General Attitude.—Based on the various aspects which have been discussed and on statements made by the 32 amputees interviewed, a composite evaluation showed the general attitude was good for 13, fair for 12, and poor for 7. The majority of those whose attitude was good were found to be experiencing less physical discomfort or symptomatology, caring for their own personal needs, living with their own family or with a relative, engaging in a more active type of recreation, and capable of ambulating in a satisfactory manner. To the extent that negative changes occurred in physical condition, mode of living, ability to get about, and restrictions in activities, the attitude tended to become fair and in a few instances poor.

Summary

A study, based on a review of hospital records and on a follow-up survey, was made on 51 amputee patients who at the time of amputation were 55 years of age or older. There was a prevalence of chronic conditions and of multiple diagnoses. The most frequent complication necessitating an amputation was gangrene for slightly under two-thirds of these amputees. After a careful evaluation, including physical condition, age, and personal and socioeconomic factors, 26 of 47 patients were fitted with prosthetic appliances while hospitalized.

Data relative to physical status at the time of leaving the hospital compared with those at the time of follow-up revealed a considerably shifting picture. For example, evidence obtained concerning those who had died indicated that a fairly large number had required further medical care, had had trouble with stumps, or had had difficulty with prosthetic appliances. Nineteen patients (37.3%) had died, 4 during the period of hospitalization when the amputation was performed and 15 after having been discharged. There was a higher incidence of mortality for those whose arteriosclerotic involvement was complicated by a diabetic condition or by cardiovascular disease.

In the follow-up survey, 32 (62.7%) former amputee patients were interviewed at their places of residence. The time intervening since the termination of hospitalization ranged from 14 to 72 months. Four men who had been fitted with prostheses were gainfully employed. In all, 22 were managing financially, usually with the assistance of various benefits.

The number of amputees living with their own family remained the most constant; twice as many were living with relatives. There was a marked drop in the number living by themselves and an increase for those in a domiciliary setting or hospital. Nineteen men were completely self-caring, nine required partial assistance, and four needed full-time care. Thirteen engaged in active and 19 in passive type of recreation.

Twenty-four of the 32 men had, by the time of the follow-up survey, been fitted with prosthetic appliances. Of these, two-thirds were using their prostheses regularly and for part of each day, one-sixth had become unable to use theirs, and one-sixth preferred not to use theirs.

Favorable morale or general attitude appeared to be related to less extensive changes regarding physical condition, mode of living, ability to ambulate, and restrictions on activities. It is believed that it was worthwhile to have given these older amputees the benefit of the use of prostheses with assistive devices in order to help them remain more functional in their self-care, ambulation, general activity, and posthospital adjustment.

13th and Harrison streets (12) (Dr. Chapman).

Virginia Bowman, medical record librarian, assisted with identification of cases and entering of initial data on work sheets for amputee patients in this study.

OBSERVATIONS ON OPHTHALMODYNAMOMETRY

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The use of the Bailliart ophthalmodynamometer makes it possible to apply increasing, measured pressure to the anesthetized sclera while the observer watches the retinal arteries. This constitutes a rapid, safe test for internal carotid artery insufficiency. Comparison of the ophthalmic artery pressures obtained when the patient is standing with those obtained when he is supine enhances the sensitivity and diagnostic usefulness of the test. Eleven cases are described to illustrate the significance of the results. Indications for ophthalmodynamometry include clinical evaluation of cerebrovascular disease and amaurosis fugax, evaluation of endarterectomies and carotid ligations, evaluation of response to anticoagulant therapy in carotid disease, and investigation prior to arteriography.

The clinical usefulness of ophthalmodynamometry in the early diagnosis of internal carotid arterial insufficiency has become increasingly important with the recent advent of more effective therapy. A dramatic reduction in the incidence of transient ischemic attacks in both the carotid and basilar-vertebral system has been reported[1] with bishydroxycoumarin (Dicumarol) and heparin-like substances. Endarterectomy[2] and other techniques have been proposed in a surgical attack on carotid atheromatous disease. The high incidence of extracranial carotid occlusion has been emphasized by the pathological studies of Fisher.[3] This has brought forth the realization that many stroke cases formerly attributed to discouraging and inaccessible vascular occlusions are not infrequently due to focal atheromatous disease in the neck.

An intensive study in cerebrovascular disease is being conducted in the Massachusetts General Hospital under the direction of Dr. C. Miller Fisher. Ophthalmodynamometry has been done in the majority of these cases and has proved of considerable value in detecting and following the course of carotid artery disease. From the data accumulated to date, several observations which appear to merit reporting have been made. These concern (1) the effects of posture on the ophthalmodynamometric diagnosis of carotid insufficiency, (2) the importance of determining systolic as well as diastolic ophthalmic arterial pressures, (3) the changes in ophthalmic artery pressure with anticoagulant therapy in carotid disease, (4) the effect of auricular fibrillation on ophthalmodynamometry, and (5) the ability to follow the effectiveness of progressive carotid ligation and of carotid endarterectomy by serial ophthalmodynamometric determinations. Perry and Rose[4] have recently reported on the correlation of ophthalmodynamometric values with the systemic blood pressure. Analysis of our data in this regard will be presented in a subsequent communication. The purpose of this report is to present the above observations and to illustrate them briefly with selected cases.

The technique of ophthalmodynamometry used throughout this study is as follows: With full mydriasis (with a 1% solution of cyclopentolate [Cyclogyl] hydrochloride) and topical anesthesia (with a 0.5% solution of proparacaine [Ophthaine] hydrochloride), an observer watches for the onset of retinal arterial pulsation and subsequently for the cessation of pulsation as an assistant exerts increasing pressure on the sclera with a Bailliart ophthalmodynamometer. The former is recorded as diastolic and the latter as systolic ophthalmic artery pressures. The observations are made by indirect ophthalmoscopy, and each end-point is checked three times for reproducibility. (Binocular indirect ophthalmoscopy facilitates testing by allowing adequate working distance for the assistant, minimizing the effect of ocular movement by means of a larger field, and possessing greater illumination and the advantages of stereopsis.) In our experience, when the pressures are within the normal range a reproducible difference of over 10 units systolic and/or 6 units diastolic has been clinically significant. This is in agreement with Hollenhorst's[5] report that a difference of 10 mm. Hg or more in the ophthalmic arterial pressures, either systolic or diastolic, indicates definite reduction of carotid flow on the side of lower pressure.

Posture Test

The possibility that postural changes might yield significant information was suggested by the fact that some patients with occlusive carotid disease

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have noted amaurosis fugax and other ischemic symptoms to be related to changes of posture. A test was proposed by one of us (D. G. C.) to study this point. It consists of measuring the blood pressure in both arms by conventional means with the patient in the supine position. The systolic and diastolic ophthalmic artery pressures are then determined by the technique given above. The patient is then placed in the standing position, and blood pressures are again taken in both arms and in both eyes.

The following four cases were selected from a larger series to show that a significant difference in the arterial pressure of the two eyes may be brought out by measurements in different positions. The significant disparity was evident when the patient was in the supine position in cases 1 and 2 and in the erect position in case 3. In the fourth case definite variations with posture were shown, but a greater disparity was seen when the patient was in the supine position initially and in the erect position three months later.

Case 1.—A 45-year-old man entered the Massachusetts General Hospital because of weakness of the left foot of 12 days' duration. Positive findings were hyperreflexia of the left knee and ankle, Babinski's response on the left, absence of all pulses below the femoral arteries, soft bruit over the left eye, increased spinal fluid protein level (66 mg. %), and a mildly diabetic glucose tolerance curve. The clinical impression was of a right internal carotid artery thrombosis with infarction in the territory of the anterior cerebral artery. Preliminary ophthalmic arterial pressures showed a lower diastolic pressure on the right side, but the values are not included in the present series because systolic measurements were not made and the effects of posture were not studied.

The patient stopped smoking, was put on a diabetic diet, and had shown a good clinical recovery when he returned four months later. At that time the following measurements were made: right arm, 140/85 mm. Hg supine and 126/76 erect; left arm, 178/90 supine and 134/70 erect; right eye, 90/43 supine and 80/40 erect; and left eye, 110/54 supine and 87/47 erect.

Comment.—This patient is believed to have had symptoms due to occlusive disease of the right carotid artery. A bruit was heard over the contralateral eye, a finding which has been previously reported in carotid insufficiency.[6] It is noteworthy that only a borderline inequality of ophthalmic artery pressures was present when the patient was in the erect position but a difference of 20 mm. Hg systolic and 11 mm. Hg diastolic was evident when he was in the supine position.

Case 2.—A 65-year-old man, with a coin lesion visible in his chest roentgenogram, developed weakness of the left hand and forearm while being prepared for thoracotomy. The monoparesis worsened over a four-hour period. On questioning, the patient recalled that previously he had had transient weakness in the left hand and two attacks of amaurosis fugax in the right eye. No ocular bruit was heard, although a bruit was audible over the right carotid artery. The visual acuity, fields, and fundi were normal. A diagnosis was made of developing right carotid thrombosis. The posture test revealed the following pressures: right arm, 130/70 mm. Hg supine and 106/68 erect; left arm, 140/80 supine and 110/70 erect; right eye, 62/30 supine and 42/25 erect; and left eye, 92/39 supine and 56/30 erect. The patient was put on bishydroxycoumarin therapy, and the left-sided hemiparesis slowly improved. Later surgical exploration revealed adenocarcinoma of the right upper lobe.

Comment.—This patient apparently developed an acute exacerbation of a chronic right carotid arterial insufficiency. The striking ophthalmodynamometric finding was a difference of only 14 mm. Hg systolic pressure when the patient was in the erect position but 30 mm. Hg when he was in the supine position.

Case 3.—A 45-year-old woman was admitted because of transient blackouts in the left eye and a history of angina pectoris. Two years previously, shortly after the death of a 37-year-old brother from myocardial infarction, the patient began having blackouts in the left eye, increasing in frequency, and subsequently occurring at least daily. They seemed to be related to sweeping, sitting up, or eating large meals. Only one attack had occurred while she was lying down, and this was mild.

Examination revealed extensive xanthelasma of the eyelids, xanthoma of various tendons, and a decreased femoral pulse rate on the right. Serum cholesterol level was 494 mg. %. A diagnosis was made of familial xanthomatosis with hypercholesteremia, atheromatosis, and occlusive left carotid artery disease. The posture test revealed the following pressures: right arm, 132/78 mm. Hg supine and 108/64 erect; left arm, 128/80 supine and 110/68 erect; right eye, 84/48 supine and 85/44 erect; and left eye, 71/42 supine and 75/40 erect. The patient was placed on bishydroxycoumarin therapy, and a marked reduction in number and severity of attacks of amaurosis fugax resulted. Repeat posture test three and one-half months after bishydroxycoumarin therapy was started revealed these pressures: right arm, 150/84 mm. Hg supine and 124/50 erect; left arm, 148/80 supine and 120/70 erect; right eye, 98/40 supine and 106/43 erect; and left eye, 71/42 supine and 75/40 erect.

Comment.—Ophthalmodynamometric measurements made prior to therapy showed approximately equal pressures in both eyes when the patient was in the supine position but a gross inequality of systolic pressure (25 mm. Hg) when she was in the erect position. After anticoagulant therapy, the ophthalmic artery pressures were elevated in both eyes but the difference in pressure persisted. This elevation of pressure with anticoagulant therapy will be referred to below.

Case 4.—A 63-year-old man complained of transient episodes of blurred vision in the right eye for two years, with headaches and transient weakness in the left arm and leg for one year. He had also had intermittent claudication of the lower extremities. General physical and neurological examination gave normal findings except for absence of a pulse in the left arm. The visual acuity and fields were normal. Ophthalmoscopy disclosed slight pallor of the right optic disk, with an enlarged cup and a small area of neovascularization at the upper nasal margin of the disk. A diagnosis of right carotid insufficiency was made. The posture test revealed the following pressures: right arm, 150/90 mm. Hg supine and 140/90 erect; left arm, pressure unobtainable in both positions; right eye, 73/26 supine and 73/21 erect; and left eye, 83/38 supine and 79/26 erect.

The patient stopped smoking, and no further attacks of amaurosis fugax or claudication occurred. A routine hemogram revealed chronic lymphocytic leukemia. Repeat posture test three months after the first measurements showed these findings: right arm, 140/100 mm. Hg supine and 136/76 erect; left arm, pressure unobtainable in both positions; right eye, 95/38 supine and 84/33 erect; and left eye, 115/41 supine and 115/38 erect.

Comment.—Although this patient was found to have mild chronic lymphocytic leukemia and simple glaucoma, his chief complaints were related to generalized atherosclerosis and particularly to occlusive disease in the right carotid, left brachial, and both femoral arteries. His symptoms of amaurosis fugax in one eye with transient hemiparesis on the opposite side are typical of internal carotid disease. Inability to obtain a blood pressure in one arm and intermittent claudication were further evidence of generalized atherosclerosis. Of greatest interest were the ophthalmodynamometric findings which, while showing a consistently lower pressure in the right eye, revealed a greater difference when the patient was in the supine position on the first examination and in the erect posture three months later.

Systolic Ophthalmic Artery Pressures

The importance of systolic ophthalmic artery pressures has only recently been stressed.[7] The diastolic values are the ones customarily given, and when there is a significant difference between the two eyes measurement of the systolic pressures may not be necessary. Although determination of systolic pressure should be done rapidly and with care, no known injury to the globe has occurred in over 100 patients in whom this measurement has been made. That systolic measurements are of considerable importance is illustrated by the following two cases of carotid occlusion in which the diastolic values were approximately the same but the systolic pressures were grossly unequal.

Case 5.—A 66-year-old man had an episode of dizziness and a partial left homonymous hemianopsia two years prior to hospitalization for a fractured femur. Recently he had lost vision in his left eye and had developed coronary heart disease. Examination showed extensive retinal arteriolar narrowing and pallor of the left disk with vision in this eye reduced to 3/200. Blood pressure measurements made only with the patient in the supine position (because of the hip fracture) were as follows: right arm, 206/108 mm. Hg, left arm, 210/110, right eye, 150+/69, and left eye, 101/67.

Case 6.—A 50-year-old woman developed a bilateral carotid-cavernous fistula after an automobile accident. This was most marked on the left side, and ligation of the left carotid artery was done first in the neck and then intracranially. The ophthalmic artery pressures in the left eye were 100/30 mm. Hg before the ligation and 50/25 after this procedure.

Comment.—Cases 5 and 6 illustrate that diastolic pressures may on occasion be approximately equal while the systolic pressures are grossly unequal. The reverse does not appear to be the case, although one patient has been encountered with a definite difference in diastolic pressures in the two eyes but with both systolic values too high to determine on the Bailliart ophthalmodynamometer.

Anticoagulant Therapy

Marked symptomatic improvement in cases of internal carotid disease has been reported from treatment with bishydroxycoumarin and heparin-like substances.[1] The means by which this is accomplished is obscure, but in case 3 findings suggested that one of the results is a partial restoration of the arterial pressure. Thus, with bishydroxycoumarin therapy, the systolic pressure on the obstructed side rose 15 mm. Hg when measured with the patient in the supine position. Findings in another patient with occlusive carotid disease studied before and after anticoagulant therapy are given in case 7.

Case 7.—A 59-year-old man complained of intermittent blurred vision in either eye, paresthesias in either hand, transient confusion, and fatigability of two years' duration. The noteworthy ocular abnormality, apart from the ophthalmic artery pressures, was a myriad of tiny microaneurysms such as we have previously seen only with atheromatous pulseless disease. These were much finer and more numerous than those of diabetic retinopathy and resembled a rete mirabile on the retina. The arteries and veins themselves were not abnormal, and the fundi were otherwise normal.

The ophthalmodynamometric values were the lowest we have encountered but were approximately equal in the two eyes and approximately the same with the patient in supine or erect positions. A diagnosis of bilateral carotid occlusive disease was made, and the patient was started on bishydroxycoumarin therapy. Four weeks later, although the prothrombin time had been reduced to only 40% of normal, he was symptomatically definitely improved. The measurements before anticoagulant therapy were as follows: right arm, 116/60 mm. Hg supine and 130/80 erect; left arm, 134/90 supine and 110/86 erect; right eye, 35/21 supine and 25/15 erect; and left eye, 28/18 supine and 25/15 erect. After four weeks of anticoagulant therapy, measurements were as follows: right arm, 134/88 mm. Hg supine and 134/58 erect; left arm, 136/88 supine and 156/92 erect; right eye, 41/28 supine and 35/24 erect; and left eye, 34/25 supine and 36/20 erect.

Comment.—This patient had extraordinarily low ophthalmic artery pressures, presumably due to bilateral carotid disease. Treatment with bishydroxycoumarin resulted in a mild but significant rise in the ophthalmic artery pressures and considerable symptomatic improvement. Definitive opinion of the possible significance of these pressure changes after anticoagulant therapy must await a larger series of cases.

Auricular Fibrillation

We encountered great difficulty in obtaining consistent readings in a patient before realizing the significance of his cardiac arrhythmia. In five other cases of auricular fibrillation, a wide and variable range of ophthalmodynamometric readings was obtained on successive testing. In these cases, both systolic and diastolic pressures may have little meaning.

Carotid Ligation and Endarterectomy

The potential value of ophthalmodynamometry in carotid ligation and endarterectomy is self-evident but curiously has been little utilized in practice. The following cases illustrate instances in which ophthalmodynamometric measurements proved of crucial value.

Case 8.—A 51-year-old woman developed throbbing pain in the right eye and eventually a total right ophthalmoplegia. Arteriography disclosed a large right carotid aneurysm in the cavernous sinus. Ophthalmodynamometry revealed a pressure of 150+/81 mm. Hg bilaterally. A Poppen clamp was placed on the right common carotid artery by Dr. Ballantine, and the pressure in the right ophthalmic artery fell to 70/40 mm. Hg while that on the left was 130/55. Five days later the patient again complained of pain in the right eye. Ophthalmodynamometry revealed a pressure of 133/52 mm. Hg in the left eye, but ophthalmic artery pressure on the right had risen to 94/50 mm. Hg. Inspection of the dressing showed that the clamp had become loose, and on reclosure the right ophthalmic artery pressure dropped to 75/43 mm. Hg within a few minutes. A tantalum band was later placed around the carotid artery, and at that procedure internal carotid arterial pressures were measured by direct manometry in the operating room while ophthalmodynamometry was performed simultaneously. Simultaneous measurements revealed the internal carotid pressure to be 80/60 mm. Hg, and ophthalmodynamometry disclosed a pressure of 81/55 mm. Hg. Five days later ophthalmic artery pressures were 67/38 mm. Hg in the right eye and 142/64 in the left. The patient improved symptomatically.

Case 9.—A 57-year-old woman suddenly developed a left-sided hemiplegia and left homonymous hemianopsia. Arteriography revealed an aneurysm of the right internal carotid artery above the bifurcation. Because of progressive worsening of symptoms a Poppen clamp was placed on the right common carotid artery by Dr. Ballantine. Mean carotid pressure by direct manometry at surgery was 62 mm. Hg, and ophthalmodynamometry two hours later revealed the pressure to be 68/50 mm. Hg in that eye. On the first postoperative day, the patient developed further paralysis of the left leg and the clamp was opened. Successive ophthalmodynamometric readings after operation were as follows: two hours, 68/50 and 150+/75 mm. Hg in the right and left eyes respectively; one day, 65/30 and 150+/52; two days (when clamp was opened), 60/30 and 130/60; three days, 62/35 and 140/59; and four days, 87/41 and 150+/65. With rise in general blood pressure and signs of cerebral edema the patient became less responsive and died. Autopsy permission was not obtained.

Comment.—These two cases illustrate the value of ophthalmodynamometry in carotid ligations. The first patient had a clamp applied to the common carotid artery, and sufficiency of the closure was indicated by ophthalmic artery pressures. A rise in ophthalmic artery pressure was noted along with recurrence of pain in the eye and led to awareness of incomplete closure of the clamp. The second patient showed a gross inequality of the arterial pressures in the two eyes, suggesting adequate occlusion, but this persisted after removal of the clamp.

Case 10.—A 51-year-old man suddenly developed a right-sided hemiplegia and global aphasia. Ophthalmic arterial diastolic pressures were 69 mm. Hg in the right eye and less than 20 mm. Hg in the left eye (*minimal scale reading*). Arteriography revealed a left internal carotid thrombosis just above the bifurcation. A left endarterectomy was performed by Dr. Kjellberg seven hours after onset of the stroke, and the next day the ophthalmic artery pressures were 150+/90 mm. Hg in both eyes. Six days later the ophthalmic artery pressures were still 134/65 mm. Hg and repeat arteriography confirmed the patency of both carotids. Twenty-two days after operation pressures were 150+/67 mm. Hg on the right and 148/71 on the left. Later, after anticoagulant therapy was discontinued, the course was complicated by the development of cortical blindness attributed to bilateral posterior cerebral artery occlusion. The ophthalmic artery pressures remained equal, and no other neurological signs consistent with carotid disease developed.

Case 11.—A 72-year-old man developed a left-sided hemiparesis and was shown by arteriography to have a right internal carotid artery thrombosis. Initial ophthalmodynamometric measurements with the patient in the supine position revealed pressure in the right eye to be 103/36 mm. Hg and in the left eye 130/55. Endarterectomy was performed by Dr. Kjellberg, and three days later the ophthalmic artery pressures were 80/34 mm. Hg on the right and 95/36 on the left. However, a cherry red spot gradually developed at the right macula, and 14 days after operation ophthalmodynamometry revealed the pressure in the right eye to be 70/42 mm. Hg and in the left eye 87/45. Repeat arteriography revealed the right carotid to be occluded.

Comment.—Cases 10 and 11 illustrate evaluation of endarterectomy. In case 10 a satisfactory restoration of equal ophthalmic artery pressures occurred and correlated well with an arteriographically patent artery. The patient in case 11, on the other hand, showed a persistently lower pressure on the operated side, and this, likewise, was consistent with the arteriographic demonstration of persistent occlusion of the carotid artery.

Summary and Conclusions

Ophthalmodynamometry is a clinical method for *determination of ophthalmic arterial pressures in* a rapid, safe fashion. Its usefulness as a diagnostic method for internal carotid arterial insufficiency appears well established. The determination and *comparison of the ophthalmic artery pressures* with the patient in the supine and the standing positions appears to enhance the diagnostic sensitivity of this test. Indications for ophthalmodynamometry are (1) clinical evaluation of cerebrovascular disease (strokes due to carotid artery occlusion, pulseless disease, aortic arch syndrome), (2) study of any case of amaurosis fugax, (3) evaluation of carotid ligations and endarterectomies, (4) evaluation of response to anticoagulant therapy in carotid disease, and (5) routine examination prior to arteriography.

Use of ophthalmodynamometry in study of cerebrovascular disease has given rise to these observations: The posture test appears to facilitate the diagnosis of carotid insufficiency in some cases. Systolic pressures should be obtained in patients in whom no unequivocal difference in diastolic values exists. Ophthalmic artery pressure in carotid artery disease may rise with anticoagulant therapy. Difficulty in obtaining reproducible values on ophthalmodynamometry should suggest auricular fibrillation or other arrhythmia. The technique is of definite clinical value in following carotid ligations and the effectiveness of endarterectomy.

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CLINICAL EVALUATION OF METHYLPHENIDATE (RITALIN) HYDROCHLORIDE IN THE NEWBORN INFANT

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Methylphenidate (Ritalin) hydrochloride is a mild central nervous system stimulant which has been administered to counteract drug-induced as well as other central nervous system depression.[1] It has been shown to be effective in shortening recovery time after light thiopental sodium–nitrous oxide anesthesia.[1k] In my experience, patients who have been depressed to a point short of unresponsiveness to verbal commands generally improve, often dramatically, after the intravenous administration of methylphenidate. More deeply depressed patients usually show some sign of lightening but not enough to awaken the patient in a short time. Respiratory minute volume was increased an average of 65% in 14 patients.

The optimum dose was found to be 0.1-0.2 mg. per pound of body weight in the anesthesia recovery time study. Very high doses were found to be less effective than the optimum.

Side-effects were limited to transient mild raising of the blood pressure and momentary nausea or retching in the clinical dose range. A dose 10 times the optimum was followed by marked tachycardia in one patient, but no tremors or convulsions were noted even after such huge doses.

Methods of Study

In order to reduce the depression of infants delivered of moderately and heavily medicated mothers, methylphenidate was administered intramuscularly in doses of 15-30 mg. to a group of 54 mothers. An attempt was made to administer it 30 to 60 minutes before delivery, but the actual time of administration varied between 3 and 498 minutes before delivery. A placebo solution was administered to a similar group of 27 patients. The principal cooperating obstetrician was impressed by the clinical improvement of the infants and complained that methylphenidate was losing its effectiveness when the placebo was substituted without his knowledge. The infants were evaluated by myself and other resident and staff anesthesiologists with respect to the onset of spontaneous and adequate respiration and of spontaneous and "good" crying (2 on the Apgar[2] scale of 0 to 2). The times for all these end-points were shorter for the methylphenidate-treated group. However, because of the wide individual variation in the medication—even though the group averages were similar—the data from these small groups were not considered suitable for rigid statistical evaluation. The study was discontinued because it was found much more practical to administer methylphenidate to the newborn infant directly, if he seemed depressed.

Methylphenidate (Ritalin) hydrochloride was administered intramuscularly to a group of 54 moderately or heavily medicated obstetric patients. It effectively reduced the depression of their newborn infants. The optimum dose appeared to be 0.1 to 0.2 mg. per pound (0.045 to 0.090 mg. per kilogram) of body weight. Subsequently it was found more practical to administer the drug intramuscularly directly to depressed infants after performing adequate oxygenation. Methylphenidate is not a substitute for oxygenation. Methylphenidate produced a marked increase in respiratory activity within 1 or 2 minutes and increased crying and body activity within 5 to 10 minutes. If the depression recurs, repeated administration of the drug is suggested. The drug produced mild side-effects, consisting in mild rise of the blood pressure and momentary nausea or retching. Methylphenidate may be used to supplement a specific narcotic antagonist, if the depression is attributable to a narcotic or to a combination of a narcotic and other depressants.

Methylphenidate, 1 mg. per 5 lb. (2.3 kg.) of body weight, was administered intramuscularly to the apparently depressed newborn infant after adequate oxygenation, with or without intermittent positive-pressure as indicated. A group of 18 babies were treated originally.

Results

Although the improvement generally noted after the administration of methylphenidate could not be attributed definitely to this agent in any given case, it was so marked and so consistent there was little doubt in my mind that the methylphenidate was effective. Within a surprisingly short time (one to two minutes), there was generally a marked increase in respiratory activity. Within 5 to 10 minutes there was usually increased crying and bodily activity, which reached a maximum in 15 to 20 minutes. Although the duration of action of methylphenidate seemed to be about three hours, the drug-depressed babies did not regress except for a return to more normal bodily activity. If such regression were to occur, the methylphenidate administration could be repeated at suitable intervals.

From Mount Sinai Hospital.

The apparently beneficial results of the methylphenidate administration were promising enough to warrant its continuation as routine treatment of depressed newborn infants in the delivery suite as well as in the nursery, especially for premature infants, even though drugs were not necessarily involved in the depression.

It should be stressed that no drug is a substitute for adequate oxygenation, which should be accomplished first. It should also be noted that a specific narcotic antagonist should be administered when the depression is due to a narcotic. However, even in these cases methylphenidate may be useful, as it seems to supplement the antinarcotic activity of the specific antagonists. When there is doubt or when other depressants are also involved, methylphenidate would be indicated in addition to the specific drug. The safety and effectiveness of methylphenidate administered to the depressed newborn infant warrants its further clinical trial.

Summary

Methylphenidate (Ritalin) hydrochloride is a mild central nervous system stimulant which appears to be free from serious side-effects. It is apparently effective in reducing depression of the newborn infant when administered to the mother, but it has been found more practical to administer it to the depressed infant directly. It appears to be safe and effective when so administered and warrants further clinical trial.

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The methylphenidate hydrochloride used in this study was supplied as Ritalin hydrochloride by Ciba Pharmaceutical Products Inc., Summit, N. J.

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CLINICAL NOTES

REACTIONS TO ORALLY ADMINISTERED POISON IVY EXTRACT

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and
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An orally administered poison ivy extract, Aqua Ivy, AP, is now being sold without prescription; each tablet contains 0.6 mg. of alum-precipitated poison ivy complex. Mass immunization of persons of varying sensitivities to poison ivy extract, without medical supervision, is hazardous, as shown by the following case summaries.

A female, aged 14, took one tablet of Aqua Ivy, AP as directed, every other day, on April 3, 5, and 7, 1958. The patient, when seen on April 9, had swelling of right wrist and elbow joints, associated with a purpuric rash of the arms and the chest. This girl, for a number of years, has suffered from severe poison ivy attacks necessitating bed rest and a physician's attendance.

The members of a family (consisting of husband and wife, both aged 41, and their sons, aged 15 and 11) each took one tablet of Aqua Ivy, AP on March 18, 20, and 22, 1958. The husband and wife both had severe generalized pruritus with headache lasting for one week. The reaction in the 11-year-old boy was essentially the same as in his parents. The 15-year-old boy started itching after the second dose, and bullae over a centimeter in diameter developed on his fingers and persisted for one week. All members of this family had a history of poison ivy sensitivity.

No other drug or infection was a factor in these four cases that would account for the symptoms after taking the poison ivy extract tablets.

Comment

The joint swelling and purpuric eruption in the first case give evidence of deep tissue and vascular reactions. Vital organs can be involved in such reactions; kidney damage has been reported.[1] The persistent headache and pruritus in adults taking the Aqua Ivy, AP is indicative of probable vascular involvement in the central nervous system.

Conclusions

Persons with a history of marked sensitivity to poison ivy should receive immunization procedures individualized for the patient. Mass desensitization procedures, without medical supervision, are dangerous.

Warwick Towers (Dr. Swarts).

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TREATMENT OF ACUTE GOUT WITH INJECTION OF COLCHICINE

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Colchicine is one of the oldest and most specific pharmaceuticals available. While newer agents such as the corticosteroids, phenylbutazone, and probenecid are valuable in the treatment of gouty arthritis, colchicine remains the most useful drug in the treatment of this disorder. Although colchicine is a remarkably safe drug, its oral administration frequently results in nausea, vomiting, and diarrhea. These manifestations act as a limiting factor and may obviate the full effectiveness of the drug. Colchicine injection is now available for intravenous administration. When the drug is given by this method, and the indicated dosage is not exceeded, gastrointestinal side-effects are rarely encountered and the response is more rapid than that obtained with the oral method. Cautious intravenous administration is also a valuable diagnostic procedure.

Report of Cases

CASE 1.—An obese 43-year-old man developed pain and swelling of the left knee eight days after an automobile accident. There was no history of trauma to the involved region. The patient denied any previous arthralgia or skeletal disease. The patient was seen the day after the onset of pain, at which time his temperature was 101 F (38.3 C) orally. The entire left knee was swollen and of a dusky red appearance. The erythema was most marked over and about the patella, which was exquisitely tender. All motion of the left knee was obviously painful. The patient was hospitalized, and the following laboratory results obtained: white blood cell count, 12,200 per cubic millimeter, with neutrophils predominating; sedimentation rate, 15 mm. per hour; uric acid, 7.35 mg. %. Shortly after admission the patient was given 2 mg. (4 cc.) of colchicine intravenously; 12 hours later he received another dose of 1 mg. (2 cc.). By this time there was moderate subjective improvement, and the patient was afebrile. Objective findings were the same. Eight hours later he again received 1 mg. (2 cc.). By this time there was marked symptomatic relief but little change in physical findings. The patient was then given 1 mg. of colchicine and 1 Gm. of probenecid to be taken orally twice daily. The patient's condition gradually improved, and he was discharged ambulant 12 days after admission.

CASE 2.—A 59-year-old man was seen at home with pain and swelling of the right knee of two days' duration. The only significant item in the patient's history was a shrapnel wound of the right knee sustained in World War I. The entire joint was quite tender, dusky red in color, warm, with marked effusion. He was hospitalized the day he was first seen. A roentgenogram taken on admission was reported as showing no significant bony abnormalities but considerable soft-tissue swelling around the joint. There was a metallic foreign body on the medial aspect of the knee joint. Urinalysis and complete blood count gave normal results. The sedimentation rate was 39 mm. per hour; uric acid level, 2.8 mg. %. An arthrocentesis was performed, and 80 cc. of straw-colored mucoid fluid was obtained. The test for uric acid gave a negative result. There were 5,000 white blood cells per cubic millimeter. The paracentesis afforded the patient considerable relief. After this he was given an injection of 2 mg. (4 cc.) of colchicine intravenously; he received 1 mg. (2 cc.) intravenously on two occasions the following day. By the time of the third injection the pain had subsided considerably; the knee remained red and tender, however, with slight recurrence of the effusion. He was then given maintenance therapy with colchicine and probenecid taken orally twice daily. His condition slowly improved, and he was discharged 10 days later, on crutches with partial weight-bearing. He had completely recovered and was ambulant four weeks after the onset of pain.

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Case 3.—A 50-year-old man was seen in the office because of swelling of the left ring finger. He had an eight-year history of recurrent migratory arthralgia and had been treated with aspirin and corticosteroids. The episodes usually lasted 5 to 10 days. To his knowledge, the diagnosis of gout had never been made. The patient was afebrile. The left third finger was swollen and red about the proximal interphalangeal joint, and there was considerable tenderness. There were no other deformities noted, and no tophi were found. The blood uric acid level was 6.5 mg. %. The patient was seen the next morning in the office and given an injection of 2 mg. (4 cc.) of colchicine intravenously. He returned the same afternoon and was given another dose of 1 mg. (2 cc.). This was repeated the morning of the third day. By that time the pain, swelling, and redness of the finger had subsided, and the only complaint was a slight stiffness. He was placed on maintenance therapy with colchicine and probenecid by mouth and continued to do well until his death from a myocardial infarction several weeks later.

Case 4.—A 55-year-old obese alcoholic man was seen in the office with a one-week history of pain and swelling of the left foot. There was no history of injury or previous joint disease. The dorsum of the right foot was swollen, red, warm, and tender; the white blood cell and differential blood counts were normal; sedimentation rate was 21 mm. per hour; uric acid, 2.75 mg.%. The patient was given an injection of 2 mg. (4 cc.) of colchicine intravenously. Later in the afternoon of the same day he received another dose of 1 mg. (2 cc.) intravenously. At that time there was slight subjective improvement. This dosage was repeated the next morning, at which time the patient was asymptomatic. The physical findings remained essentially unchanged. Therapy was started with probenecid and colchicine by mouth, and when the patient was seen two weeks later the foot appeared normal.

These four cases illustrate the diagnostic and therapeutic advantages of intravenously administered colchicine. In two of the above cases the uric acid level was within normal limits, and the intravenous injection of colchicine confirmed the clinical impression of gouty arthritis. None of the patients experienced any undesirable gastrointestinal disturbances. One individual had a mild thrombophlebitis of the vein in the left antecubital space, which subsided rapidly. No other toxic effects were noted.

Summary

Intravenous administration of colchicine is a rapid, safe, and uncomplicated method of treating acute gouty arthritis. It is of special value as a diagnostic procedure in those cases where the diagnosis of gout is doubtful, because of its rapid action and freedom from the nausea, vomiting, and diarrhea often found with oral administration.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following paper, which was presented by Dr. Warren H. Cole as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on The Use and Abuse of Adrenal Steroids. This is the fifth paper in the series, the first four of which appeared in The Journal *on June 20 and 27 and July 4 and 11, 1959, pp. 952, 1063, 1179, and 1311.*

H. D. Kautz, M.D., *Secretary.*

STEROID THERAPY IN SURGICAL PATIENTS

John H. Schneewind, M.D.
and
Warren H. Cole, M.D., Chicago

The increased use of steroids in the treatment of general medical problems has been paralleled to a moderate extent by the increased use of these drugs for surgical patients in the preoperative and postoperative periods, as well as during operative procedures. In our experience, there are three situations in which steroid therapy is indicated. The first is in acute severe injury or illness in which acute adrenal insufficiency is suspected because of a significant fall in blood pressure not explained by blood loss or coronary disease. In many instances it is difficult to be sure that these patients have a true adrenal insufficiency, and, if they recover, it is not always clear whether steroid therapy was responsible. Admittedly, this is not a very common situation. The second category of patients in whom steroid therapy is indicated are those who have been receiving steroid medication for arthritis or colitis for weeks

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or months. It is necessary to assume that the patient may have some degree of adrenal suppression and that cortisone (Cortisone, Cortogen, Cortone) acetate and hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) will be needed in the immediate operative period to prevent an acute adrenal insufficiency. A third type of patient in whom steroids may be useful is the chronically ill, malnourished person who has no desire for food. Some of these patients regain their appetite, eat well, and have a general feeling of well-being after administration of corticotropin (ACTH, Acthar, Corticotropin, Cortrophin). Frequently, a significant weight gain, with positive nitrogen balance, seems to improve their ability to withstand the stress of operation.

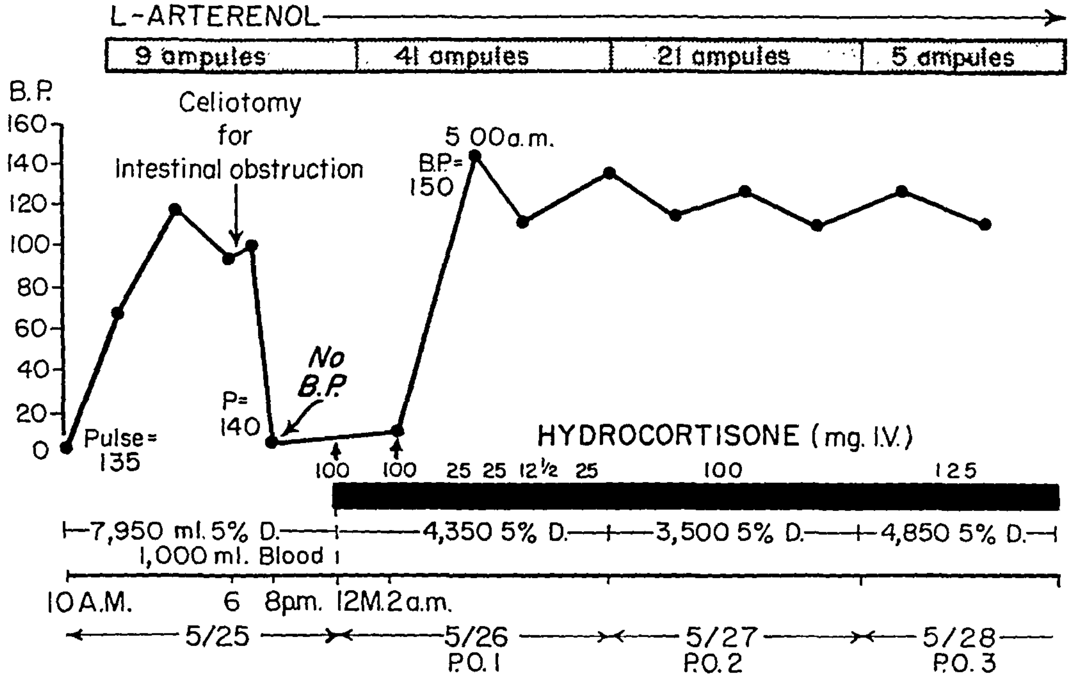

Fig. 1.—Patient with prolonged severe hypotension treated with levarterenol bitartrate and hydrocortisone sodium succinate.

Adrenal Insufficiency due to Acute Illness or Injury

Significant hypotension which cannot be explained by acute blood loss, myocardial infarction, anesthesia, drugs, or electrolyte imbalance should suggest the possibility of an acute adrenal insufficiency. This is especially true if the blood pressure does not respond promptly to blood transfusions or vasopressors.

Adams and Siderius[1] have reported on five patients with postoperative shock in whom they felt the diagnosis of adrenal insufficiency was justified. One patient had persistent hypotension and tachycardia after removal of a hydronephrotic kidney. In the immediate postoperative period the hypotension became severe, despite adequate blood, fluid, and electrolyte therapy. Levarterenol (Levophed) bitartrate was given continuously but was ineffective. On the third postoperative day hydrocortisone sodium succinate (Solu-Cortef) was given intravenously, and the blood pressure rose sharply and gradually stabilized. The patient received a total of 250 mg. on the third day and 200 mg. on the fourth day. No levarterenol was required. The patient recovered and was discharged on the 14th postoperative day. Adams and Siderius suggest that an increase in capillary resistance and potentiation of the effect of vasoconstrictors on blood vessels may be factors in the blood pressure response to adrenal corticosteroids. However, they warn that epileptic seizures or psychotic reactions may be precipitated by administration of steroids.

Howland and associates[2] reviewed the statistics covering a one-year period at the Memorial Center for Cancer and Allied Diseases and reported that 25 cases, or approximately 1 out of every 300 patients subjected to operation, exhibited some form of adrenal cortical insufficiency. They reported in detail on seven cases. One patient with a bronzed skin was thought to have had a previously unrecognized adrenal cortical hypofunction; one patient had been taking cortisone for several months prior to operation, and one patient had had bilateral adrenalectomy and oophorectomy for metastatic breast cancer. The other patients had no obvious reason for adrenal insufficiency. All of the patients exhibited persistent hypotension and failed to respond to adequate blood replacement and vasoconstrictors. Respiratory depression and prolonged reaction time after anesthesia also occurred. All seven of the patients reacted favorably and rapidly after intravenous administration of soluble hydrocortisone. Howland and colleagues[2] believe that the basic physiological disturbance was a deficiency of adrenal cortical secretion.

Hayes[3] has studied the endocrine response to stress of normal patients and of patients with limited adrenocortical reserve. Most of the patients were subjected preoperatively to either the epinephrine-eosinophil response or the corticotropin-eosinophil (Thorn) test. Ordinarily, increased adrenal cortical output is reflected in a decrease in the numbers of eosinophils and lymphocytes in the blood. Hayes believes that an elevated eosinophil count during stress is direct evidence of an insufficient supply of adrenocortical hormone. If the patient is in shock that is unresponsive to adequate blood replacement and if the eosinophil count is not at the anticipated low level, a condition of temporary adrenocortical insufficiency is present and should be treated with steroids administered intravenously.

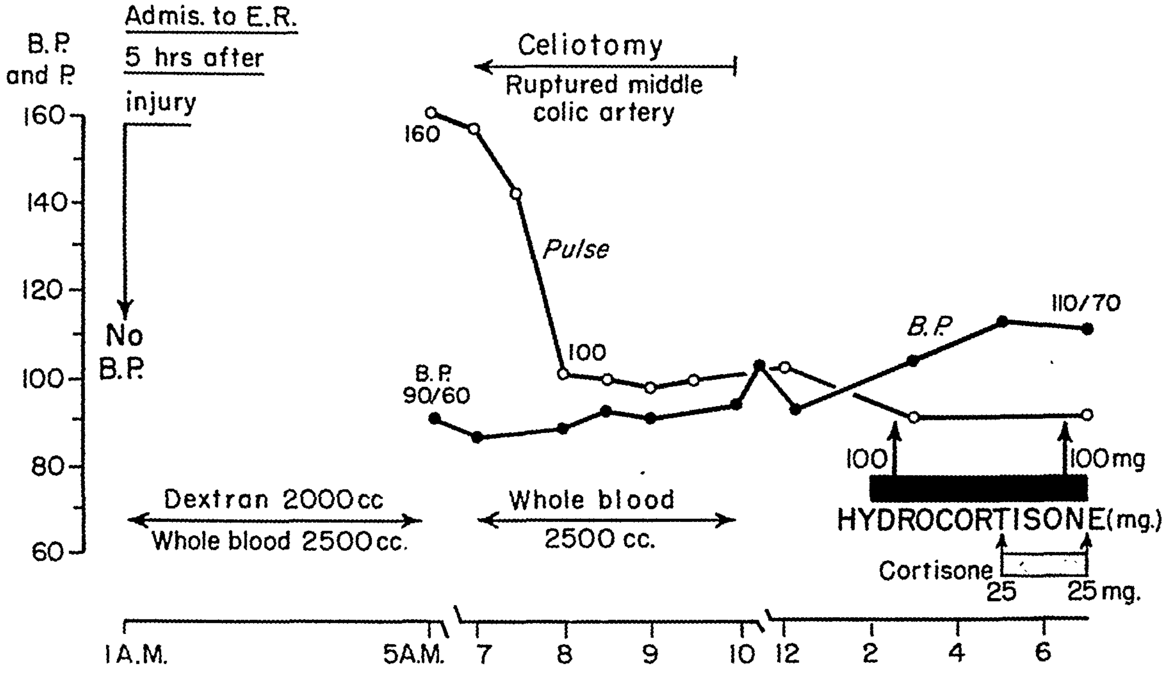

Fig. 2.—Recovery record in patient after massive hemorrhage due to blunt trauma. Hydrocortisone given intravenously seemed of benefit in stabilizing blood pressure and improving pulse.

An example of our experience with this type of problem may be illustrated by the case of a 47-year-old woman who was admitted to the hospital because of cramping abdominal pain, distention, and vomiting for four days (fig. 1). She was obviously acutely ill, with a distended abdomen and only occasional bowel sounds. Her blood pressure was unobtainable. Although the patient's sensorium was depressed, she was able to answer questions and give a coherent history. Soon after admission a Levin tube was passed, and immediately a great deal of gastric content was returned. Fluids containing levarterenol were given intravenously, but it was not until four hours after admission that a blood pressure reading was obtained. Eight hours after admission the patient was taken to the operating room. Celiotomy confirmed the diagnosis of obstruction of the small intestine, which was secondary to adhesions in the pelvis due to previous operations. The patient tolerated the operation fairly well, but soon after reaching the recovery room the blood pressure was again unobtainable. Despite the fact that levarterenol was given continually after the operation, the blood pressure continued to be unobtainable. At midnight, four hours after operation, 100 mg. of hydrocortisone sodium succinate was administered intravenously, and another 100 mg. was given about two hours later. At the same time, the quantity of levarterenol administered was increased. At 2 a. m. the blood pressure was still unobtainable. At 5 a. m., approximately five hours after administration of the first dose of hydrocortisone sodium succinate, the blood pressure was 150/80 mm. Hg, and, although it fluctuated a good deal, it remained at satisfactory levels. An additional 87.5 mg. of hydrocortisone sodium succinate was administered on the first postoperative day, making a total of 287.5 mg. of that drug. The patient received a total of 82 mg. of levarterenol during this period. On the second postoperative day, 100 mg. of hydrocortisone sodium succinate was given, and it was possible to maintain the blood pressure with about half of the amount of levarterenol previously required. On the third postoperative day, the patient received 125 mg. of hydrocortisone sodium succinate and 10 mg. of levarterenol. On the fourth and fifth postoperative days, the patient received 80 and 45 mg. of hydrocortisone sodium succinate, respectively, but no levarterenol was required (fig. 1).

The patient's postoperative course was uncomplicated, except for a severe slough of the skin on the lower half of the right leg at the site of administration of the levarterenol. This area was treated in routine fashion and eventually was covered with split skin grafts.

Another example of temporary adrenocortical insufficiency is that of a 51-year-old man who was admitted to the hospital five hours after an automobile accident in which he had been struck in the abdomen by the steering wheel (fig. 2). On admission to the emergency service, no pulse or blood pressure was obtainable. After administration of two liters of dextran (Dextran, Expandex, Gentran) and 2,500 cc. of whole blood, the blood pressure was 90/60 mm. Hg and the pulse rate 160 per minute. The patient was taken to the operating room, and a celiotomy revealed a ruptured middle colic artery which was spurting vigorously. There was a great deal of blood in the peritoneal cavity, marked cyanosis of the transverse colon, and extravasated blood in the mesocolon. The patient received an additional 2,500 cc. of whole blood during the operation. His pulse rate gradually subsided to about 100; however, the blood pressure remained at 90 mm. Hg. The middle colic artery was ligated, and a transverse colostomy was performed.

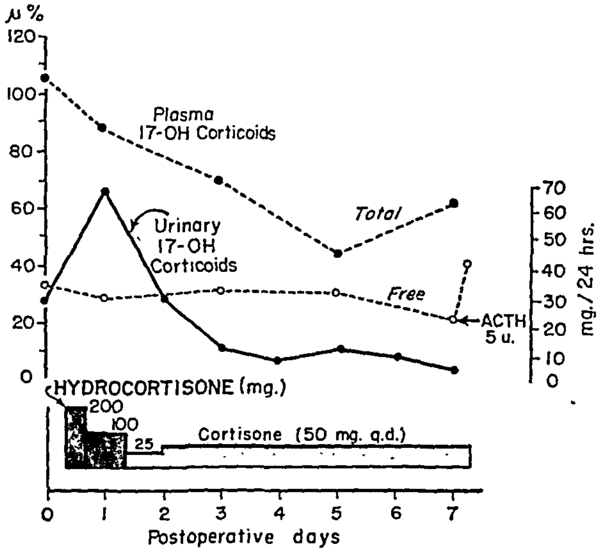

Fig. 3.—Steroid output of patient with massive hemorrhage due to blunt trauma.

Although the patient tolerated the procedure moderately well, his blood pressure remained low, his skin was cool, and his peripheral pulse was of poor quality. Four hours after the end of the operation, 100 mg. of hydrocortisone sodium succinate was added to the intravenous fluids (fig. 2). During the next two hours the patient's systolic pressure rose, and the pulse slowed to 80 per minute. The patient received a total of 300 mg. of soluble hydrocortisone intravenously during the remainder of the first postoperative day.

The patient developed a spiking fever due to pneumonitis three days after operation. The fever gradually subsided, however, and the patient's postoperative course otherwise was fairly good. He was readmitted to the hospital a month later for closure of his colostomy, which was tolerated without incident. This patient's steroid output during the immediate postoperative period was studied, and a graphic representation of our findings is shown in figure 3. The initial determination of plasma corticosteroids was made on blood drawn during operation. The elevated total plasma corticosteroid level of 106 mcg. per 100 cc. is probably related to oliguria due to the long period of hypotension. The free plasma corticosteroids, on the other hand, were at normal levels throughout the immediate postoperative period. The subsequent values for the total plasma and urinary corticosteroids reflected the intravenous administration of hydrocortisone sodium succinate. On the seventh postoperative day, a 5-unit test dose of corticotropin was administered, and one hour later the patient's free plasma corticosteroids had risen from 20 to 38 mcg. per 100 cc. This is consistent perhaps with an active adrenal reserve and ability to respond to stressful stimuli.

Preparation of Patients on Prolonged Steroid Therapy for Operation

It is well known that prolonged steroid therapy will produce adrenal atrophy and that patients with adrenal cortical insufficiency tolerate the stress of operation when given adequate doses of steroids. The administration of corticosteroids should be continued during the operative period and during the immediate postoperative period. Schwartz and associates[4] studied the records of 19 patients with adrenal cortical insufficiency subjected to operation. Three deaths occurred in this series, and none of these three patients had received specific hormone therapy prior to or during operation. Hypotension occurred in 14 patients during anesthesia or in the postoperative period, and it occurred with the same frequency regardless of the anesthetic agent used. They feel that agents which may produce significant hypotension are inadvisable and warn of the necessity for an alert watch for hemorrhage and excessive trauma during operation.

In a review of the problem of administration of anesthetics to patients who have been receiving steroids, Lundy[5] was one of the first to emphasize that, since prolonged administration of cortisone may result in atrophy of the adrenal cortex, patients who have been receiving this medicament must be properly prepared for operation. He feels that the anesthesiologist should be able to recognize the atypical picture of shock which may occur during anesthesia and operation and should be prepared to treat this with appropriate steroid therapy.

In a comprehensive review of the problems of postoperative adrenal insufficiency, Root[6] cites several reports concerning adrenal insufficiency produced by administration of cortisone. One study showed a diminution of the average weight of 46 adrenal glands at autopsy in patients who had been given cortisone, as compared with a control series of patients who had not been receiving cortisone. The author also points out that circulatory collapse not related to blood loss and not responding well to transfusions and vasopressors may occur not only during or shortly after operation but up to one or two days later. He states that usually there is an unexpected degree of mental confusion which may be followed by disorientation and coma. Subnormal temperature and profuse sweating have also been noted.

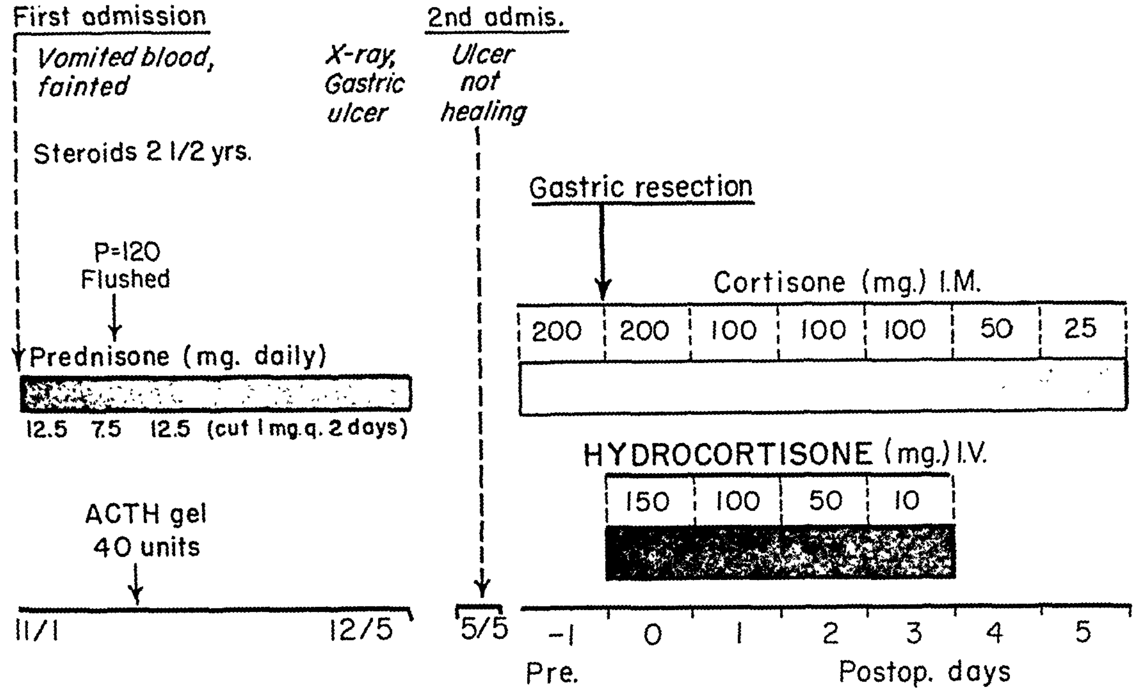

Fig. 4.—Steroid management of patient operated on for gastric ulcer. Administration of steroids was required because patient had been receiving them for arthritis for two and one-half years.

Engleman and associates[7] attempted to determine the degree of cortical suppression after steroid therapy by studying 19 patients who had been receiving maintenance doses of cortisone for 12 to 26 months. These patients showed a response to stimulation on the third to sixth day of corticotropin therapy, whereas control patients responded on the first or second day. They conclude that, although adrenal function may be suppressed by long-term cortisone therapy, the suppression is usually reversible. It must be remembered, however, that a markedly increased demand, as in a patient undergoing operation, might not be covered by adequate adrenal function. In general, it is probably a safe rule that any patient who has received steroid therapy for five days or more during the year preceding operation should receive prophylactic treatment to prevent adrenal cortical insufficiency during an operative procedure.

The problem of management of a patient undergoing steroid therapy who experiences a sudden onset of upper gastrointestinal hemorrhage is presented by the case of a 43-year-old woman who entered the hospital because of hematemesis on the day prior to admission (fig. 4). This patient had suffered from rheumatoid arthritis for 19 years and had been receiving cortisone for approximately 2½ years prior to admission. The cortisone therapy had been changed recently to prednisone (Deltasone, Deltra, Meticorten, Paracort), 12.5 mg. daily. On the day before admission the patient had been doing her housework when suddenly she became dizzy and fainted. On regaining consciousness she found that she had vomited bright red blood. Roentgenographic studies revealed evidence of arthritic changes, most marked in the hands, and a large ulcer-crater deformity along the greater curvature of the midantrum. The patient was placed on an ulcer regimen, and the prednisone dose was reduced to 7.5 mg. Because of tachycardia, flushing of the face, extreme weakness, and thirst, the amount of prednisone was increased to the original dose of 12.5 mg. It was then gradually reduced by 1 mg. every two days and finally discontinued completely. The patient subsequently developed bilateral conjunctivitis which responded to an ophthalmic preparation of hydrocortisone. Although repeated upper gastrointestinal x-rays showed some healing of the ulcer, complete healing had not yet occurred approximately six months after the initial episode of hematemesis. At this time, it was felt that celiotomy was indicated.

The patient was prepared for operation and received 200 mg. of cortisone acetate intramuscularly the day prior to and again on the day of operation (fig. 4). The patient received 100 mg. of cortisone acetate daily on the first, second, and third postoperative days, 50 mg. on the fourth, and 25 mg. on the fifth postoperative day. The patient also received hydrocortisone sodium succinate intravenously on the day of operation and on the first, second, and third postoperative days. A gastric resection was performed, which the patient tolerated very well. Her postoperative course was uneventful and on discharge she was receiving aspirin for her arthritis but was not on any steroid medication.

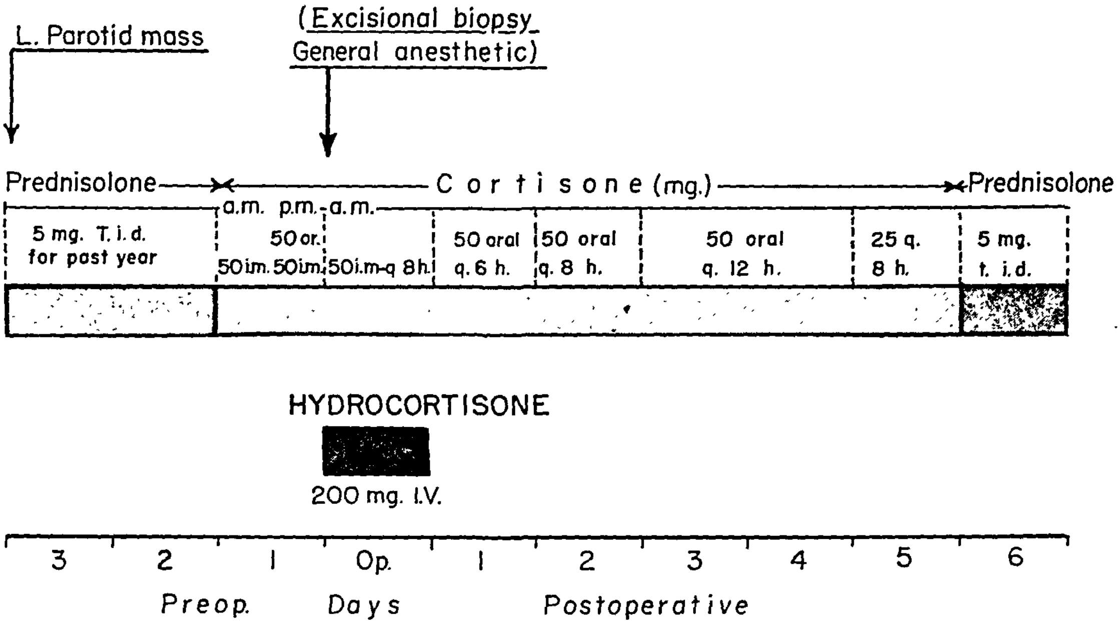

Fig. 5.—Steroid management of female patient during operative period. Patient had been receiving prednisolone for one year prior to admission.

Another example of a strong indication for steroid therapy during the immediate operative period occurred in a woman, aged 57, who had been receiving prednisolone (Delta Cortef, Hydeltra, Meticortelone, Paracortol) for the past year. She entered the hospital because of a mass in the left preauricular area which had been increasing in size during the month prior to admission. Approximately 18 months prior to this admission, the patient had had a laminectomy. At this operation a lymphoblastoma covering the dura from T-2 to T-6 was found. The patient had received radiation therapy and a course of nitrogen mustard postoperatively. During the year prior to admission, she had been receiving 15 mg. of prednisolone daily. Physical examination revealed a mass 4 by 4 cm. in the left preauricular area. There also was a 1-cm. mass just posterior to the angle of the mandible. Because of the history of removal of a lymphoblastoma from the spinal canal, it was felt that excisional biopsy of the small lymph gland was indicated. Since the patient was to receive a general anesthetic, her steroid management was planned as for any major operation. The details are shown in figure 5. The prednisolone therapy was continued until the day before operation and then discontinued. On this day the patient received 50 mg. of cortisone acetate intramuscularly in the morning and evening as well as 50 mg. of cortisone acetate orally. On the day of operation the patient received 50 mg. of cortisone acetate intramuscularly before operation and every eight hours thereafter. Prior to induction of anesthesia, 100 mg. of hydrocortisone sodium succinate was added to a liter of 5% dextrose injection and administered intravenously. The patient received soluble hydrocortisone by slow drip throughout the operation and during the rest of the day until midnight, at which time she had received a total of 200 mg. On the first postoperative day the patient was given 50 mg. of cortisone acetate orally every six hours; this was decreased to 50 mg. orally every eight hours on the second postoperative day. The patient received 50 mg. of cortisone acetate every 12 hours on the third and fourth postoperative days and, finally, 25 mg. every 8 hours on the fifth postoperative day. On the sixth day the cortisone therapy was discontinued, and the patient was put back on prednisolone therapy, 5 mg. three times daily (fig. 5).

The patient tolerated the anesthetic and the excisional biopsy without incident and was discharged on the seventh postoperative day. The biopsy specimen revealed metastatic lymphoblastoma, and it was planned to treat her with additional radiotherapy.

Use of Corticotropin in Preoperative Preparation

Treatment of Disease Process.—There is a group of cases in which corticotropin or cortisone may be very effective in improving operability by reducing the serious effects of the disease itself. The two best examples of these diseases or conditions are ulcerative colitis and thrombocytopenic purpura. It is well known that treatment with corticosteroids will cause marked improvement in most patients with these two diseases; it is equally well known that subsequent courses of therapy are decreasingly effective. Accordingly, when patients are acutely ill with either of these two diseases, many clinicians adopt the principle of reducing the manifestations with steroids and then resorting to operation, providing the patient has had ulcerative colitis for at least six months and has other evidence of intractability. Since the benefit of steroid therapy in ulcerative colitis is transient, many clinicians avoid the prolonged use of steroids because, if conservative therapy fails, the surgeon may be compelled to operate, with the patient in a very critical condition. This was the situation with the patient illustrated in figures 6 and 7; the acute manifestation of her disease responded quite well to steroids initially, but, as time passed, cortisone was not effective. Perforations of the colon necessitated an operation, but the patient was in an extremely hazardous condition. She survived the operation but died in the postoperative period. If a colectomy had been performed early, during the initial benefit from steroids, she might have been alive today.

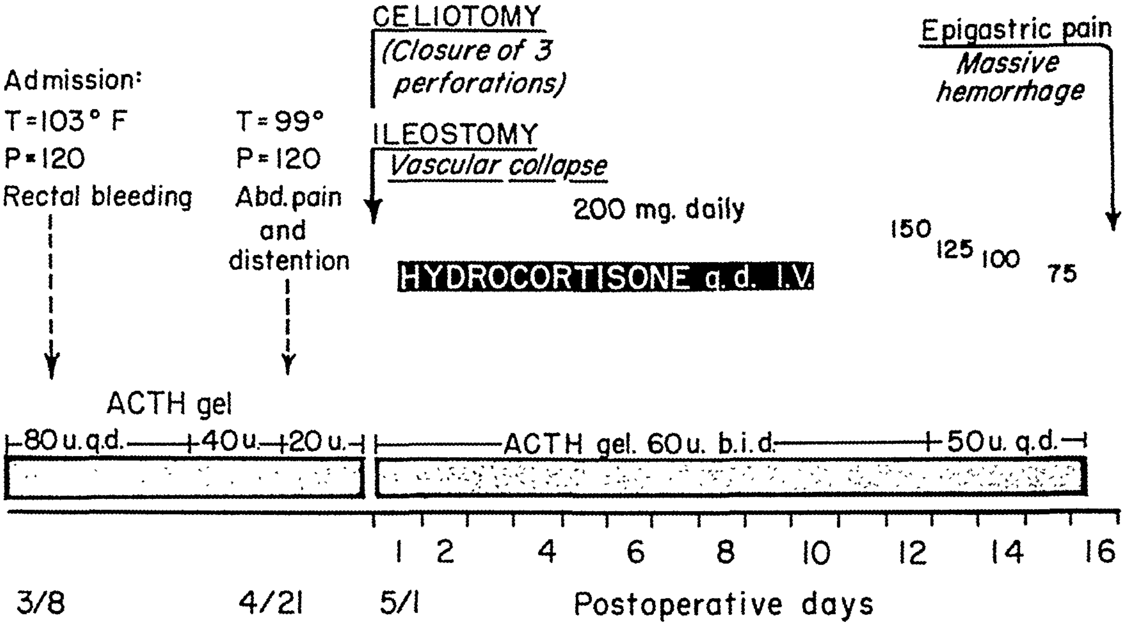

Fig. 6.—Management of patient with severe ulcerative colitis complicated by perforations. Acute vascular collapse during surgery necessitated intravenous administration of hydrocortisone. Drug continued during immediate postoperative period.

Improvement of Appetite and Sense of Well-being.—In selected patients, corticotropin may be of great value in improving appetite, increasing food intake, and producing a feeling of well-being.[8] It is true that some of the weight gain after corticotropin therapy is due to water retention, but the increased food intake often results in elevation of blood protein levels, positive nitrogen balance, and a general improvement of the mental status of the patient about to undergo an operation.

Galante and associates[9] regard corticotropin as an antipyretic and euphorigenic agent. They state that the drug may permit early ambulation, may effect an increase in appetite and sense of well-being, and may decrease the postoperative requirements of narcotics. The authors also discuss the value of corticotropin as an anti-inflammatory agent in such diseases as ulcerative colitis and regional enteritis. They point out that suppression of fever, toxicity, and malaise may result in considerable improvement of the patient prior to operation.

Corticotropin occasionally may be of value in patients with a smoldering rheumatic activity requiring valvuloplasties. The drugs also may be of value in certain allergic or hypersensitive states such as hemolytic anemia and thrombocytopenic purpura, with or without hypersplenism. In the immediate preoperative period, administration of corticotropin may result in a decrease of hemolysis and an increase in the platelet count. Corticotropin and the other steroids also have a place in the treatment of serum sickness and drug and transfusion reactions. In certain cases of nontropical sprue, the adrenal steroids may be effective in producing a remission characterized by improved appetite, increased dietary intake, weight gain, and a decrease in the number, fat content, and watery consistence of the stools.[10]

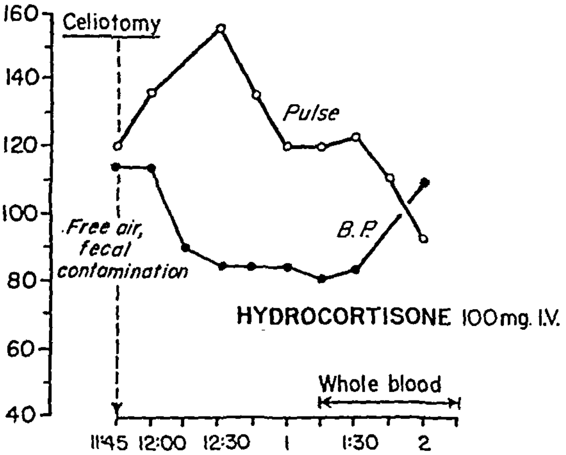

Fig. 7.—Pulse and blood pressure during operative period of patient with severe ulcerative colitis complicated by colon perforations. Hydrocortisone seemed to be of value in elevating blood pressure and reducing pulse rate.

The following history illustrates the use of corticotropin for the purpose of improving appetite and increasing food intake. A 60-year-old woman entered the hospital because of intermittent attacks of pain in the upper part of the abdomen. Approximately four months prior to admission, the patient experienced two attacks of moderately severe pain in the right upper part of the abdomen accompanied by chills and fever. The pain extended to other parts of the abdomen and radiated to the back, and she occasionally suffered from excessive gaseousness and eructation. The patient was fairly well after these attacks, except for a recurrent mild attack approximately two weeks prior to admission. She had lost 11 lb. (5 kg.) during the six months prior to admission. There was no history of jaundice, dark urine, or pale stools. Because of the chills and fever, both an intravenous urogram and a retrograde study were performed. It was the impression of the urologists that the kidneys were normal. A cholecystogram revealed calculi in the gallbladder.

Although the patient claimed she ate well, she failed to gain weight during the first week in the hospital. It was felt that she would benefit from an increased food intake, and corticotropin gel, 80 units daily, was given intramuscularly on the eighth day after admission to the hospital. The patient's weight increased from her admission weight of 115 lb. (52.2 kg.) to a peak of 122 lb. (55.4 kg.) during the six days of corticotropin administration (fig. 8). At this time a cholecystectomy was performed which was tolerated well. The patient's postoperative course was essentially uneventful. After the operation the body weight dropped to a low of 112 lb. (50.9 kg.) on the sixth postoperative day but then began to increase slowly until the patient was discharged. There was a marked increase in 17-hydroxycorticosteroid output by the adrenals after administration of corticotropin prior to operation (fig. 9). The total plasma corticosteroids rose to a peak of 147% and the free corticosteroids to 97%. The total urinary corticosteroids also increased to 82 mg. for 24 hours. These values were recorded after the first two days of steroid therapy.

Another example of the use of corticotropin in improving food intake prior to operation is that of a 64-year-old male who was admitted to the hospital with a history of scleral icterus two and one-half months prior to admission. The patient noted that his stools had become pale and his urine dark. He also complained of epigastric fulness, poor appetite, and easy fatigability. There was a 20-lb. (9-kg.) weight loss during this period. The noteworthy findings on physical examination were the obvious jaundice and a palpable liver and gallbladder. Laboratory studies were consistent with the findings of obstructive jaundice. The patient's alkaline phosphatase and bilirubin levels were elevated; the albumin-globulin ratio was 4.1:2.6; and there was mild anemia.

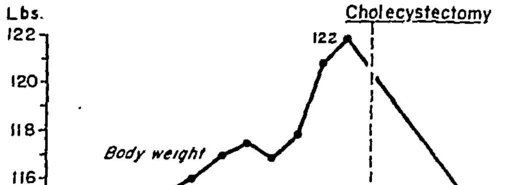

Fig. 8.—Body weight curve after administration of corticotropin in 60-year-old woman.

During the patient's first 10 days in the hospital, he did not eat well because of anorexia and a feeling of fulness in his abdomen after taking small amounts of food and liquid. Because of the failure to gain weight, the patient was started on therapy with 40 units of corticotropin intramuscularly, twice daily. A four-day course of this therapy was given, and the patient's body weight increased from 137 to 143 lb. (62.2 to 65 kg.) (fig. 10). His daily caloric intake increased by approximately 1,200 calories. At operation a large tumor mass consistent with carcinoma was found in the head of the pancreas. A cholecystojejunostomy was performed, with an entero-enterostomy below it. The patient's postoperative course was complicated by severe bronchial pneumonia, with high temperatures. On the eighth postoperative day the pneumonia subsided, and the patient appeared much improved. During this period the icterus had subsided appreciably. The patient's body weight declined during the postoperative period because of the pneumonia but began to increase again after the infection had subsided.

Contraindications and Complications of Steroid Therapy

There are certain contraindications to the routine use of steroid therapy for surgical patients. These include the presence of tuberculosis, malignant hypertension, uremia, psychoses, and the presence of active ulceration in the gastrointestinal tract. Other points which require consideration are the possibility of spread of localized infection, prevention of wound healing, fluid retention, and glycosuria and hypoglycemia due to the anti-insulin effects of corticotropin and cortisone. As a rule, these problems are not encountered during short-term administration of the steroids but become manifest when large doses are administered for periods exceeding seven days.[9]

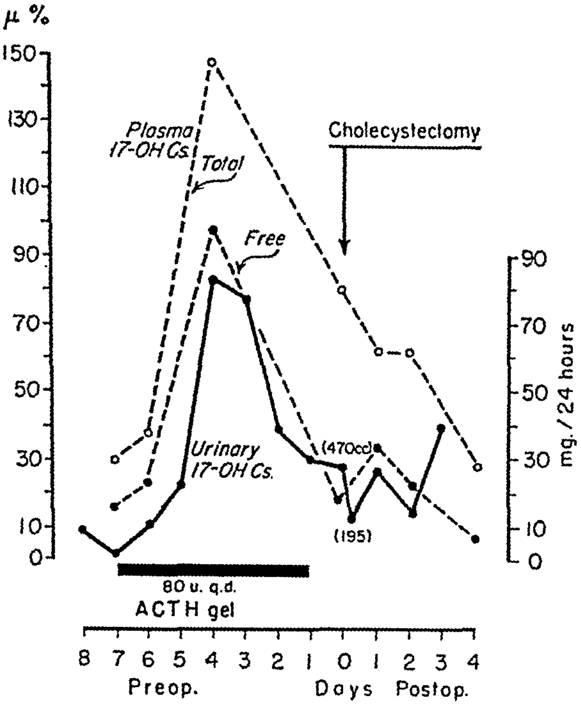

Fig. 9.—Effect of administration of corticotropin on plasma and urinary 17-hydroxycorticosteroids.

In a review of the use of corticotropin and adrenal corticosteroids in diseases of the digestive system, Zetzel[10] states that ulcers rarely develop in patients receiving steroids. He feels that the possibility of the development or even the knowledge of a preexisting peptic ulcer is not an absolute contraindication to an otherwise valid indication for steroids. With respect to perforation of the intestine and hemorrhage, he states that several large series of cases have been reported in which these complications were no more frequent than in control series of patients who were not receiving steroids. However, not all those persons working with steroids would agree with these statements.

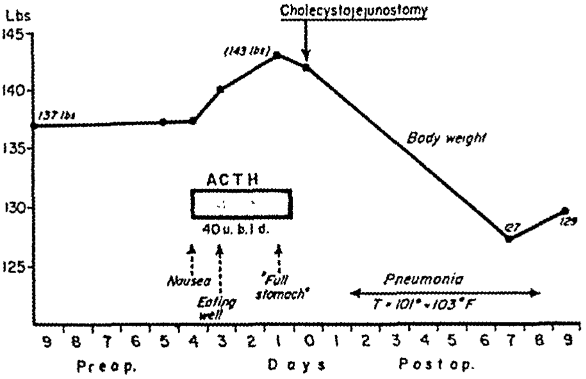

Fig. 10.—Weight gain in patient with obstructive jaundice after administration of corticotropin.

The following complicated case history illustrates several of the problems which may arise in treating surgical patients with steroids. This case history includes intestinal perforation, vascular collapse on the operating table, steroid therapy during operation and in the immediate postoperative period, and, finally, massive hemorrhage, possibly due to steroids. Brief reference has already been made to this patient (fig. 6). She was a woman, aged 32, admitted to the hospital with a history of ulcerative colitis characterized by intermittent episodes of diarrhea, with mucus and blood, for a period of 10 years. Because of exacerbation of the bloody diarrhea, the patient was admitted to the medical service. At this time she was acutely ill, markedly malnourished, and was passing blood through the rectum. Sigmoidoscopy revealed polypoid changes in the rectum. An attempt was made to improve the patient's condition by giving her transfusions, antispasmodics, sedatives, and steroids in the form of corticotropin gel, but the patient continued to lose ground. Approximately one month after admission she experienced a sudden onset of abdominal pain, distention, and tachycardia, probably due to a perforation of the colon (fig. 6). Her condition was so critical it was felt that celiotomy could not be tolerated, and it was elected to treat her with gastrointestinal siphonage and antibiotics, in the hope that the perforated intestine would seal over. This apparently happened; however, 10 days later the patient again had signs and symptoms of a perforation of the colon. Plain films of the abdomen showed a large amount of air under the diaphragm, and it was felt that celiotomy must be undertaken.

At operation a large amount of fecal contamination and three large perforations of the colon were found. The perforations were closed, and an ileostomy was performed. During the operation the patient exhibited signs of an acute vascular collapse; however, the blood pressure improved after administration of blood and hydrocortisone sodium succinate (fig. 7). The patient continued to be in very critical condition after the operation. She received hydrocortisone, corticotropin, a liter of protein hydrolysate, and 500 cc. of cottonseed oil (Lipomul I. V.) daily. Several units of human serum albumin and whole blood were given. She gradually improved until, on the seventh day after operation, she was able to take liquids by mouth. Two weeks after the operation the patient suddenly developed a spiking fever associated with a shaking chill, and soon afterward dark blood appeared from the ileostomy. A Levin tube was inserted, and approximately 200 cc. of dark blood was obtained from the stomach. At this time the patient complained of severe pain in the epigastric area. Shortly afterward the patient sustained a massive hemorrhage and died. Permission for a postmortem examination was refused.

As may be noted in figure 6, this patient received corticotropin gel as part of the treatment of the severe exacerbation of her disease, and this may have been a contributing factor leading to the colon perforation. The severe vascular collapse during operation was probably due to the combined effects of malnutrition, sepsis, and adrenal insufficiency, but it responded to blood and hydrocortisone given intravenously. The patient improved after operation until the sudden onset of a fatal gastrointestinal hemorrhage. It is entirely possible that the operative stress and steroids resulted in a peptic ulcer and the terminal hemorrhage.

Comment

It seems clear that certain acutely ill or injured patients may exhibit signs of adrenocortical insufficiency during or after an operation. In the first example presented (fig. 1), a previously healthy patient with a severe intestinal obstruction remained in a shock-like state despite massive intravenous fluid therapy. It was not until hydrocortisone sodium succinate was administered that the blood pressure rose to normal levels and remained relatively stable.

The value of hydrocortisone in major surgery has been reviewed by Rukes and associates.[11] They found the drug useful in patients requiring bilateral adrenalectomy, in patients with adrenal insufficiency after major surgery, and in patients in shock unresponsive to standard therapy. A total of 50 patients of this type were treated, usually for no longer than five days. No complications of the treatment were noted.

Patients who have been on long-term steroid therapy and require operation certainly are more prone to adrenal insufficiency than is the average patient. Preparation for operation with steroids is not difficult and need not be extended for prolonged periods after operation. It is true that some of these patients might tolerate operation without steroids being given preoperatively; however, we believe it is much safer to prepare them all with steroids in order to prevent an unexpected adrenal insufficiency during or immediately after operation.

We have found corticotropin helpful in improving operability in selected patients by causing a marked improvement in appetite, increased food intake, and feeling of well-being. It by no means produces these effects in every patient. In general, those patients with lesions of the mouth or jaw or with obstructive lesions of the gastrointestinal tract are not suitable for this type of therapy. Now that intravenous solutions of fat and of concentrated protein hydrolysate are available, it is not difficult to effect weight gain by this parenteral therapy prior to operation. We believe it is preferable to achieve increased food intake and weight gain by the oral route if possible, and corticotropin may provide just the additional stimulus needed to bring certain patients into optimal preoperative condition.

Summary

The most important condition in which steroids are useful in treating surgical patients is that of acute adrenal insufficiency after severe injury or illness. The most prominent sign of this condition is persistent hypotension which cannot be explained by blood loss or coronary disease and which does not respond to adequate blood replacement. In these conditions, rapid, adequate therapy with hydrocortisone administered intravenously may be lifesaving. Patients requiring operation who have been on long-term steroid therapy present the hazard of adrenal depression and an acute insufficiency during operation. We believe that the safest procedure is to prepare all of these patients with steroids prior to operation. Corticotropin may be of value before operation by effecting a feeling of well-being and increasing appetite and food intake. Other beneficial effects of corticotropin include suppression of fever, toxicity, and malaise in conditions such as regional enteritis, and diminution of hypersensitive reactions in hemolytic anemia or thrombocytopenic purpura. Under such circumstances, when operation is contemplated in patients acutely ill with ulcerative colitis or purpura (less commonly with regional enteritis), administration of corticotropin may result in so much improvement that operation is made safe instead of being extremely hazardous. Contraindications to the use of steroids include active tuberculosis, malignant hypertension, uremia, psychoses, and the presence of active ulcers in the gastrointestinal tract.

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DEATH OF THE FETUS IN UTERO.—The woman is definitely aware of . . . her pregnancy from the moment that she feels life. . . . She keeps careful watch on the fetal movements, and her obstetrician asks about them and routinely checks the fetal heart sounds. . . . Life inside stirs her imagination. . . . All of a sudden, she realizes that she has not felt the fetal movements for a few hours or even a day. She becomes panicky and immediately calls the obstetrician. No matter how busy he may be . . . it is imperative that he see her at once. It may be a false alarm. Many are, and if so, there will be great relief. But if the fetal heart has stopped beating, and he is unable to hear it, he is there . . . to confirm the fact, to transmit it gently and to be of comfort. . . . We can be of the greatest help if we run over . . . in our mind's eye the psychological factors that all at once begin to shake the patient: loss of status, a sense of failure, loss of confidence and courage, frustration, disappointment and sorrow. Many questions will be asked. The answers must be honest and compassionate. We must search to explain the cause of death. Was it diabetes, toxemia, anoxia from a tight cord around the neck, trauma? The cause of death must be explained. . . . The patient must be absolved of guilt, else she will brood and think dark thoughts that may injure her self esteem. She may over-react and blame herself for doing that forbidden chore, for washing floors on hands and knees contrary to the advice of in-laws, for taking a long automobile ride, for getting unduly excited over some problem. . . . Some women blame sexual intercourse for the death and project all their wrath upon their husbands, creating a wound in their marriage that will be difficult to heal. The obstetrician must eliminate doubt and guilt, be sympathetic about this setback and optimistic about the future. . . . The responsibilities of her doctor have not ended, however. . . . All thoughts must be centered on her safe deliverance. . . . It must be explained . . . that we must wait for nature to initiate the birth process, for artificial interference may lead only to trouble and greater misfortune. She should be told that when a baby dies in utero and remains undelivered for some time, fibrinogen depletion may cause postpartum hemorrhage. But there are reliable tests for this condition, and an adequate supply of blood is available if transfusion becomes necessary.—A. D. Elia, M.D., The Management of Grief Situations in Obstetrics, *The Boston Medical Quarterly*, March, 1959.

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HEALTH PROBLEMS IN EDUCATION

THE fitness of youth has interested the American physician for a long time. At the first American Medical Association meeting in 1848 a standing committee was established to "present an annual report" on a number of items, among which were educational institutions "and their relations to the laws of life." Thirty years later a committee of the Association further resolved that medical men ought to have a voice in the health aspects of the construction and location of public school buildings. The committee also felt physicians should have something to say about the age at which children should be admitted, the hours of study, and the general management of these institutions as these relate to health and expressed the belief that one or more physicians should serve on boards of education, boards of trustees, and similar boards having control of education and schools.

Among the instrumentalities for carrying out this expressed interest has been the Joint Committee on Health Problems in Education which the American Medical Association shares with the National Education Association. For nearly a half-century it has expressed the interest of physicians in education and the cooperation of educators and physicians by passing resolutions and preparing publications concerned with the health of children, school health and safety, and health education.

The entire process of elementary and secondary education has been subjected to a critical reevaluation during the decade known as the "atomic era" and, more particularly, in the "post-sputnik" period. There has been increased emphasis on the "three R's" and the physical sciences particularly. Physics and mathematics have dominated the educational scene, sometimes to the neglect of the biological sciences, health education, and physical education. To emphasize the essentiality of placing health education and physical education in proper perspective in the curriculum, the Joint Committee on Health Problems in Education reaffirmed its belief in the need for including these in the curriculum of elementary and secondary schools. The Joint Committee urged the employment of teachers especially qualified to teach health by reason of special preparation in health education and the acceptance of a comprehensive instruction program including such areas as nutrition, safety, first aid, body care, prevention of disease, community health, consumer education, mental health, emotional health, dental health, the deleterious effects of alcohol, tobacco, and drugs, and other important topics relating to life and living. Sufficient instructional time was suggested to allow for a stimulating and challenging program. This would mean at least the equivalent of a daily period for one year in junior high school and one year in senior high school.

Physical education as well as health education is an essential factor in the development of our youth. Because of the rather universal acceptance of physical activity as a desirable factor in physical, mental, emotional, and social well-being and in the maintenance of health, the Joint Committee on Health Problems in Education urged boards of education, school authorities, and physical education personnel to provide adequate facilities and suitable personnel for the development of physical education programs that would be an integral part of the school curriculum. Such instruction would develop a variety of activity skills and abilities for all boys and girls. Cooperation with other community agencies would assure broad opportunities for participation in vigorous physical activities both in and out of school hours for all pupils.

To further emphasize the physician's role in the entire health and physical education program, practicing physicians were urged by the Joint Committee to stimulate their colleagues' interest in and support for comprehensive programs of health education, health service, physical education, and athletics in the school. Physician interest in these areas of health science will insure the medical soundness that can be given only by medical understanding and supervision of activity programs. In fact, the Joint Committee on Health Problems in

Education and the National Conferences on Physicians and Schools, sponsored by the Department of Health Education of the American Medical Association, exist to help promote a closer relationship between physicians and the educators administratively responsible for our schools. Only by physician interest and concern can the health protection of our children be assured.

School transportation is a problem in health protection and accident prevention. With an increase in use of the school bus comes an increase in the school day, in the period of inactivity required of children, in the increased contacts with infectious material, particularly streptococci, and in the exposure to hazards of highway travel. With these problems in mind, the Joint Committee on Health Problems in Education recommended that every effort be made consistent with safety to avoid excessive time spent riding the school bus and to prevent children who are ill from riding the bus. Furthermore, the necessity was recognized for keeping the bus clean, comfortable, well-ventilated, and appropriately heated and for compliance with existing state and federal laws and regulations regarding the safe operating conditions of the bus, essential first-aid equipment, and fire extinguishers. The Committee also recommended that every bus driver should be required to have a physical examination at least annually and to otherwise conform to standards generally accepted for operators of commercial vehicles.

The American Medical Association's Council on Industrial Health called the attention of the Joint Committee to carbon tetrachloride as a toxic agent. This solvent is carefully regulated in industry to protect employees against hazardous overexposure. Yet this dangerous chemical is commonly found in laboratories and classrooms used in teaching chemistry and physics. It enters into experiments involving evaporation, solution, and other similar problems, and in the automotive and other shops of the school it is used as a degreasing agent. A resolution of the Joint Committee on Health Problems in Education called the attention of school administrators and teachers to the hazards associated with carbon tetrachloride, particularly since it is sometimes termed a "safety" solvent because it is not flammable, and some science textbooks and manuals call for its use without adequate warning of its hazards or a statement of the precautions to be taken for its safe use. The Committee also wished to call the attention of the publishers of science textbooks to this danger.

Protecting the health of our children and youth, and instructing them in the principles of healthful living, is a never-ending job. While the physician's responsibility in this task was recognized more than a century ago, today it is as true as then that physicians, educators, and the various professions in public health must work together to maintain the maximum protection and provide the optimum instruction. The contribution of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association is but one of many such contributions being made by these two professions, but it is a significant one which has been going on for nearly a half-century.

ALL DUES-PAYING MEMBERS WILL RECEIVE THE JOURNAL AND A SPECIALTY JOURNAL

The House of Delegates at the Atlantic City meeting in June endorsed a new policy adopted by the Board of Trustees whereby all dues-paying members of the Association will receive The Journal and one of the A. M. A. specialty journals as a dues-paying membership benefit. Dues-paying members may select any one of the 10 A. M. A. specialty journals in the fields of internal medicine, surgery, ophthalmology, children's diseases, otolaryngology, pathology, dermatology, industrial health, neurology, or psychiatry. Thus, in all, such members will receive as a benefit of membership an A. M. A. specialty journal of their choice, *Today's Health, The AMA News,* and The Journal. Since the range of The Journal extends across the entire field of medicine, the House of Delegates and the trustees believe that all members of the Association should receive The Journal in addition to the specialty journal of their choice.

The dues-paying members who are not now receiving The Journal because they chose to receive a special journal will begin receiving The Journal within a few weeks. The 142,000 dues-paying members who already receive The Journal will receive an announcement asking them to choose one of the 10 scientific monthly journals, which will then be sent to them when their choice is made known to the Circulation and Records Department.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

MEDICAL NEWS

ARKANSAS

Symposium on Trauma.—The Union County Medical Society will sponsor a Symposium on Trauma given by the department of surgery, Washington University, School of Medicine, St. Louis, on Sunday, July 26, at the Randolph Hotel Building, El Dorado, Ark. A Flying Physician's breakfast is planned for 8:00 a. m. The following papers by St. Louis authors are scheduled:

Intraabdominal Injuries, Dr. James M. Stokes.
Head Injuries, Dr. William S. Coxe.
Thoracic Injuries, Dr. Charles L. Roper.
Hand Injuries, Dr. Arthur H. Stein Jr.
Injuries to the Genitourinary Tract, Dr. Charles H. Nicolai.
Spinal Cord Injuries, Dr. Coxe.
Injuries to the Peripheral Blood Vessels, Dr. Stokes.
Blood and Fluid Replacement in Trauma, Dr. Harvey R. Bernard.

The afternoon session will include a motion picture, a paper, "Relationship of Civil Defense to the General Practitioner," by Mr. Owen Payne, state civil defense chairman, and a concluding panel discussion conducted by Dr. Stein. For information write Dr. Berry L. Moore, 218 Masonic Temple Building, El Dorado, Ark.

CALIFORNIA

Dr. Hayes Honored.—Dr. Edward W. Hayes Sr., associate professor of thoracic diseases, College of Medical Evangelists, Loma Linda and Los Angeles, received the annual alumni achievement award from the Alumni Association of Carleton College, Northfield, Minn., for "distinguished service to the medical profession and devotion to the College." Only 48 persons in the history of the 93-year-old college have received the honor. Dr. Hayes is a past-president of the American College of Chest Physicians.

Society News.—The California Society of Plastic Surgeons held its ninth annual meeting April 9-11. The new officers for 1959-1960 are: president, Dr. George V. Webster, Pasadena; vice-president, Dr. Harry M. Blackfield, San Francisco; secretary-treasurer, Dr. Richard A. Shepard, Oakland; and historian, Dr. James B. Johnson, Beverly Hills.——The new officers of the Los Angeles Pediatric Society are: Drs. Morris J. Naiditch, president; Lawrence S. Siegel, vice-president; and Neil N. Litman, secretary-treasurer.

Personal.—Dr. Arild E. Hansen, chairman, department of pediatrics, University of Texas Medical School, Galveston, was appointed research director at Children's Hospital of the East Bay, Oakland, succeeding Dr. Irvine McQuarrie, who will continue as research consultant. Dr. Hansen will assume his duties in midsummer.——Dr. Charles M. Stewart, Los Angeles, who has been secretary-treasurer of the Western Section, American Urological Association, for the past six years, was unanimously voted president-elect of the section for 1961. Dr. John W. Dorsey, 125 E. 8th St., Long Beach, was elected the new secretary-treasurer.

Department of Virology.—A new department of virology was established on the Berkeley campus of the University of California. It is reportedly one of the first departments in any major university to be dedicated to the study of viruses and will be closely associated with the 10-year-old Virus Laboratory on the Berkeley campus. Chairman of the new department is Dr. Wendell M. Stanley, Nobel Laureate and director of the Virus Laboratory. Eight faculty members, drawn from the laboratory, comprise the staff of the department. Starting in September, lecture courses will be offered to graduate and advanced undergraduate students, to be followed later by a comprehensive laboratory course. Additional instruction will be offered, mostly at the graduate level, in the form of special study courses, seminars, and research projects. The main objective of the teaching program in virology will be to provide persons well grounded in biology, chemistry, or physics with "intensive specialized instruction" in the biochemical, biological, and biophysical aspects of virology. No change is anticipated in the over-all research program of the Virus Laboratory. The program of formal courses and research will lead to the master of science degree with a major in virology, or to the doctor of philosophy degree. The department is now accepting applications from qualified students. A limited number of teaching and research assistantships are available.

COLORADO

Report on Building Program.—The $17,500,000 building program proposed for the University of Colorado Medical Center was aided with recent action by the Colorado Legislature's Joint Budget Committee in approving the development of detailed plans. The six-man body unanimously approved an expenditure of $239,000 for development

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

of the plans. The proposed building program calls for a new 400-bed hospital, a research building, a dental school, and expanded space for the School of Medicine and the School of Nursing. It will require about 1½ years to complete the plans. Meanwhile, additional legislature hearings will be held to discuss methods of providing the necessary state funds required for the project. The Medical Center currently has $6,000,000 in building mill levy funds for the project, and a matching grant of $1,300,000 from the U. S. Public Health Service.

CONNECTICUT

Dr. Richards Becomes General Manager.—Dr. William R. Richards, Hamden, assumed full-time duties in the newly created post of general manager of the Connecticut State Medical Society. He was appointed to the new position after having served one year as part-time executive secretary of the society. Dr. Richards has discontinued his medical practice in obstetrics and gynecology in New Haven, where he has had an office since 1946. He is a past-president of the New Haven Obstetrical Society and a diplomate of the American Board of Obstetrics and Gynecology.

State Medical Election.—Dr. Ellwood C. Weise, Bridgeport, assumed office as president of the Connecticut State Medical Society and was succeeded as president-elect by Dr. John N. Gallivan, East Hartford, at the annual meeting of the society. Other officers elected included: Drs. G. Gray Carter, Greenwich, first vice-president; Roy C. Ferguson, Rockville, second vice-president; Isadore S. Goldberg, Torrington, treasurer; William R. Richards, New Haven, executive secretary and general manager; and Denis S. O'Connor, New Haven, managing editor of *Connecticut Medicine,* the society's official publication.

ILLINOIS

Chicago

Aid for Disabled Physicians.—The Adolph Gehrmann Fund of the Chicago Community Trust provides for financial aid to practicing physicians who are in need of financial assistance while regaining their health. Their widows may be eligible for assistance for not more than one year following their physician-husband's death. Apply to Chicago Community Trust, 10 S. LaSalle St., Chicago 3.

Society News.—Dr. Theodore R. Van Dellen, associate professor of medicine, Northwestern University Medical School, was named president-elect of the Chicago Medical Society at the society's council meeting recently. Dr. George C. Turner, designated president-elect in 1958, was installed as president for 1959-1960 on June 24, succeeding Dr. Edwin F. Hirsch. Dr. Patrick H. McNulty was reelected secretary.——Officers for the 16th season (1959-1960) of the Chicago Surgical Society were elected at the annual business meeting May 22 as follows: Dr. John L. Keeley, president; Dr. John V. Prohaska, vice-president; Dr. Robert L. Schmitz, secretary; Dr. Burton C. Kilbourne, treasurer; Dr. Tracy H. Clarke, recorder; and Drs. Francis H. Straus, John M. Dorsey, and Charles B. Puestow, councilors.

Chairman for Physiology Department.—Prof. Dwight J. Ingle, Ph.D., hormone researcher, was appointed chairman of the University of Chicago's department of physiology, effective July 1. He succeeds Prof. Nathaniel Kleitman, Ph.D., who has been acting chairman of the department since the resignation of Prof. John O. Hutchens Sept. 30, 1958. Drs. Kleitman and Hutchens are professors of physiology. Earlier this month, Professor Ingle returned from a tour of research centers in Russia sponsored by the U. S. Public Health Service Institute of Arthritis and Metabolic Diseases. The discoverer of the biological effects of the hormones cortisone and hydrocortisone, Professor Ingle was the George S. Cox Medical Research Fellow at the University of Pennsylvania from 1938 to 1941. He holds the 1947 award of the Laurentian Hormone Conference in Biology and the 1948 W. E. Upjohn Prize.

Personal.—Dr. Gilbeart H. Collings Jr., medical director of Crane Co., Chicago, since 1957, following service with the U. S. Army Medical Corps at the Army Environmental Health Laboratory, was appointed to the new position of associate director of the medical department of Standard Oil Company (Indiana). Previously he had been with the Tennessee Valley Authority as chief of the occupational health branch, and with Bethlehem Steel Co.——Dr. Percival Bailey, professor of neurology and neurological surgery and clinical professor of psychiatry, University of Illinois College of Medicine, will retire from the university on Sept. 1 and become full-time director of research at the new Illinois State Psychiatric Institute.——Dr. Frederick E. Vultee Jr. was appointed associate director of the Rehabilitation Institute of Chicago. Dr. Vultee was formerly an associate professor of physical medicine and rehabilitation at the Medical College of Virginia, Richmond.

International Awards for Film.—Two international awards for excellence of a scientific film were presented to Dr. Hans Von Leden, assistant professor of otolaryngology, Northwestern University Medical School, and G. Paul Moore, Ph.D., lecturer in the same department. The U. S. Department of State sent notice of the awards recently, although the film festivals were held several months ago. The film, "The Larynx and Voice—Laryngeal Physiology Under Daily Stress," was one of 320 entries in the fourth International Review of Scientific Films held in Rome. All branches of science were represented at the film festival. Dr. Von Leden's film was awarded the Gold Medal of the Italian Red Cross and was one of the few films of a medical subject to receive a prize. This was presented to the United States representative in Rome and was reportedly the only major prize won by the United States at this festival. The second award was won at the Third International Review for Scientific Education at the University of Padua under the sponsorship of the international film festival in Venice. The award to the Northwestern scientists was for "education in the field of medicine." They were also presented with a bronze ox head—the traditional gift at the University of Padua for awards of merit. During the past three years, Drs. Von Leden and Moore have won five international awards for their work in laryngeal physiology.

NEW JERSEY

Fitkin Hospital Symposium.—On July 18, Fitkin Memorial Hospital Day, a medical symposium will be held at the hospital in Neptune. The program includes the following papers and speakers:

Fetal Distress—Evaluation and Management, Dr. Alan F. Guttmacher, New York City.
Clinical Experiences with Pancreatitis, Dr. John M. Howard, Philadelphia.
Newly Isolated Viruses in Respiratory Disease, Dr. Robert H. Parrott, Washington, D. C.
Pulmonary Hypertension, Dr. Richard S. Ross, Baltimore.

The general chairman for the symposium is Dr. Samuel H. Rubin, Director, Department of Medical Education, Fitkin Memorial Hospital, Neptune, N. J. Information on the symposium may be obtained by writing Dr. Rubin.

NEW MEXICO

Summer Clinic in Ruidoso.—The New Mexico Academy of General Practice will present the Ruidoso Summer Clinic July 20-23 in Ruidoso, with headquarters at the Navajo Lodge. Four panel discussions are planned: "Steroids Today," "Psychosomatic Medicine," "Low Back Pain," and "Orthopedic and Urological Complication in Obstetrics." The program will include the following papers:

Common Fractures in General Practice, Dr. Arthur L. Glassman, Houston, Texas.
Office Gynecology, Dr. Stanley F. Rogers, Jr., Houston, Texas.
Management of Orthopedic Difficulties of the Newborn, Dr. Glassman.
Evaluation of Cephalo-Pelvic Disproportion, Dr. Rogers.
Management of Urinary Tract Infection, Dr. Abel Leader, Houston, Texas.

For information, write Dr. Owen C. Taylor Jr., Publicity Chairman, Ruidoso Summer Clinics, Fourth and Washington, Artesia, N. M.

NEW YORK

State Medical Election.—Dr. Norman S. Moore, of Ithaca, was chosen president-elect of the Medical Society of the State of New York by the House of Delegates at its 153rd annual meeting. Dr. Moore will serve for one year after which he will become president, succeeding Dr. Henry I. Fineberg, of Jamaica, who was installed as president. Dr. Fineberg succeeds Dr. Leo E. Gibson, of Syracuse. Also elected were Dr. John L. Sengstack, of Huntington, vice-president, and Dr. William L. Wheeler Jr., of New York City, secretary.

Personal.—Dr. Irvin Klein was appointed medical director of the New York State Workmen's Compensation Board. Dr. Klein, of New York City, has been an associate examining physician of the board since 1942. He succeeds Dr. Willis M. Weeden.—Richard H. Barnes, Ph.D., dean of the Cornell University Graduate School of Nutrition, Ithaca, was appointed editor of the *Journal of Nutrition.* He succeeded George R. Cowgill, Ph.D., of the Yale Nutrition Laboratory, who served as editor for 20 years. Cyril L. Comar, Ph.D., director of the Laboratory of Radiation Biology, New York State Veterinary College, has been appointed associate editor.

Reorganize Mental Hospital.—A program of reorganization is in process at Pilgrim State Hospital, Dr. Paul H. Hoch, New York State Commissioner of Mental Hygiene, announced. Under the new plan the 14,000-bed hospital will be decentralized into a cluster of 2,000- to 3,000-bed units each under the management of an assistant director who will discharge both clinical and administrative functions for the unit. Each division will be self-contained and will have its own admission service, treatment facilities, and release procedures. Certain of the institution facilities will be shared, however, such as the transportation and maintenance pools, the business office, etc. Plans for the reorganization have been worked out by Dr. Henry Brill, recently appointed director of Pilgrim. Preliminary work on the project began about a year ago. Two of the small units have already been established.

New York City

Dr. Swan Named Department Head.—Dr. Roy Craig Swan Jr. was named professor and head of the department of anatomy, Cornell University Medical College, by the board of trustees. He is also treasurer of the New York State Society for Medical Research.

Research and Library Building.—Cornell University received a grant of $1,600,000 from the Samuel J. and Evelyn L. Wood Foundation of New York. The grant, together with a matching grant of $1,300,000 from the United States Public Health Service, will be used toward the construction of a research and library building for the Cornell University Medical College. Cost of the new building will be about $3,200,000. The new building, a seven-story structure at 1300 York Avenue, will be named the Samuel J. Wood Library and Research Building. It will provide the Medical College with about 50,000 square feet of additional space, which will be used by Cornell students and faculty and by staff members of the Sloan-Kettering Institute, New York Hospital, Memorial Hospital, the Cornell University-New York Hospital School of Nursing, Hospital for Special Surgery, and the Rockefeller Institute. Samuel J. Wood, after whom the new building will be named, and his wife established the Wood Foundation in 1958 with the objective of furthering medical research in this country.

Dedicate Rehabilitation Wing.—Dedication ceremonies opening the new $500,000 Maurice B. Hexter Rehabilitation Wing at Beth Abraham Home for the Chronic Ill, 612 Allerton Ave., the Bronx, were held June 23. Mayor Robert F. Wagner, speaking at the ceremonies, pointed out the city's pilot "Homestead Plan" and program to help the chronic disabled and aged. Undertaken at the suggestion of Dr. Howard A. Rusk, the program provides 1856 beds in five separate institutions located in different parts of the city. The new rehabilitation center is named for Maurice B. Hexter, Ph.D., executive vice-president of the Federation of Jewish Philanthropies of New York. The wing houses the division of physical medicine and rehabilitation including the departments of physical therapy, hydrotherapy, electrotherapy, occupational and speech therapy, recreation, and music. The new rehabilitation center is housed on the ground floor of Beth Abraham's recently opened $3,500,000 Henrietta and Stuard Hirschman Pavilion. Beth Abraham Home, a 531-bed nonprofit institution, is affiliated with and receives its major philanthropic support from the Federation of Jewish Philanthropies.

OHIO

Training Positions in Infant Neurology.—Training in developmental pediatrics and infant neurology is available for board eligible physicians at the Clinic of Child Development of the Children's Hospital, Columbus, on two levels. The first is a fellowship for physicians, preferably pediatricians, recently completing their residencies, with an opportunity to continue at faculty status in the teaching and research program. American citizenship is required. For those with additional qualifications, whether in pediatrics or in other fields, there is available a full-time staff appointment in the department of pediatrics of the Ohio State University College of Medicine, with major responsibility in teaching and research. For information write to the Clinic of Child Development, Children's Hospital, 561 S. 17th St., Columbus 5, Ohio.

PENNSYLVANIA

Dr. Hess Gives Annual Doyle Lecture.—The second annual Dr. Joseph A. Doyle memorial lecture was given April 30, at Thiel College, Greenville, by Dr. Elmer Hess, Erie. The title of the lecture was "The Future of Medicine In the United States." Dr. Doyle, to whose memory the lectures series is dedicated, was a surgeon in the Greenville area from 1920 until his death in 1947. He was one of founders and a member of the staff of the Medical Center Clinic of Greenville. The lectures "represent an effort on the part of Medical Center Clinic to honor Dr. Doyle, while promoting interest in the medical program offered at Thiel College." Dr. Hess is a past-president of the American Medical Association, Pennsylvania Medical Society, and the American Urological Association. He has served as chief of staff at St. Vincent's Hospital, Erie, since 1941.

TEXAS

Medical Assembly in Houston.—The 25th annual meeting of the Postgraduate Medical Assembly of South Texas will be held July 20-22 at the Shamrock Hilton Hotel, Houston. The program will include lectures under medical and surgical specialties. Luncheon speakers will include Dr. Walter C. Alvarez, Minneapolis; Dr. Alton Ochsner, New Orleans; and Dr. F. J. L. Blasingame, Executive Vice-President, A. M. A., Chicago. Other guest speakers include the following:

> Drs. Fred H. Allen Jr. and Charles L. Schepens, Boston; A. E. Braley, Iowa City; Louis Thomas Byars, St. Louis; George F. Cahill, New York City; Tague C. Chisholm and Charles A. Neumeister, Minneapolis; J. Brown Farrior, Tampa, Fla.; Francis L. Lederer, Chicago; Donald B. Lucas, San Francisco; Vincent Moragues, Omaha; H. M. Pollard, Ann Arbor, Mich.; Clyde L. Randall, Buffalo, N. Y.; Robert N. Rutherford, Seattle; Wiley Mitchell Sams, Miami; Louis J. West, Oklahoma City, Okla.; Lawrence E. Young, Rochester, N. Y.; and Morton Fuchs, Philadelphia.

Technical and scientific exhibits and a program of medical motion pictures are planned, and a program of entertainment is arranged. Registration fee is $25. For information, write the Postgraduate Medical Assembly of South Texas, 412 Jesse H. Jones Library Building, Houston 25, Texas.

WASHINGTON

Housing for Hospital Staff.—Contracts for the 39-unit University Hospital staff housing project at the University of Washington, Seattle, to be financed by a loan from the Federal Housing and Home Finance Agency, were awarded by the university's board of regents. The project is budgeted at $400,000, including contingencies, fees, and taxes, and will be self-sustaining on the basis of rentals. The apartments will provide quarters for married interns and residents who must be on 24-hour call at the new University Hospital. Completion date will be about Dec. 1.

WISCONSIN

Dr. Haessler Retired.—Dr. Ferdinand Haessler, Marquette University School of Medicine's first full-time professor in the clinical departments, retired July 1. Dr. Haessler has been chairman of the department of ophthalmology since Jan. 15, 1949, when an anonymous benefactor established the first full-time chair of ophthalmology. Dr. Haessler devoted his time to the management of the eye clinic and dispensary in the medical school, to teaching, and to the development of a training program for physicians interested in a career in ophthalmology.

Dr. Rath Named Medical History Chairman.—Appointment of Dr. Gernot B. Rath, of the University of Bonn, Germany, as chairman of the history of medicine in the University of Wisconsin Medical School, Madison, was approved by university regents June 9. Dr. Rath, who will have the rank of associate professor, had been visiting professor of medical history during the second semester of the 1958-1959 school year. The appointment is effective Jan. 1, when Dr. Rath will return to Wisconsin from Germany. The Wisconsin Medical School reportedly was a pioneer in the field of medical history teaching and research, setting up a department for that purpose in 1950. Two other European-trained scholars have participated in the program. Dr. Erwin H. Ackerknecht served as chairman from 1950 to 1957. He came to Wisconsin in 1947 as the first professor of medical history in the Medical School. Dr. Walter Artelt, of the University of Frankfurt, was visiting professor of the history of medicine in 1958.

GENERAL

Japan's First Woman Physician Dies.—Dr. Yayoi Yoshioka, 88, Tokyo, Japan's first woman physician and founder of the Tokyo's Women's Medical School, now Tokyo's Women's Medical College, of which she was president, died May 23. She had taught at the Medical School and College for more than 50 years and had helped to establish hospitals in Tokyo.

Postpone Examination in Nuclear Medicine.—The board of trustees of the American Board of Radiology has decided to postpone the obligatory examination in nuclear medicine until after June 30, 1962, for those candidates being examined in radiology or therapeutic radiology. Up until that time, therefore, the examination in nuclear medicine will be optional for those who wish to be examined in radiology or therapeutic radiology.

Medical Degree Stolen.—The medical degree of Dr. John Philip Brady, Tillamook, Ore., under the date of June 15, 1925, given by the University of Michigan Medical School, Ann Arbor, has been stolen. Dr. Brady was licensed in Minnesota in 1929 and in Oregon in 1954. These are the only states in which he is licensed to practice. Persons having knowledge of the stolen degree should notify Mr. Howard I. Bobbitt, Executive Secretary, State of Oregon Board of Medical Examiners, 609 Failing Building, Portland 4, Ore.

Dr. Grantly Dick Read Dies.—A pioneer of "natural" childbirth techniques, Dr. Grantly Dick Read, died at his home in Wroxham, England, June 11. He was 69. Dr. Dick Read practiced as a gynecologist in London from 1923 to 1948. In 1949 he went to Johannesburg, South Africa, to set up a world center for childbirth without pain. His books include "Childbirth Without Fear," "Introduction to Motherhood," and "No Time for Fear." In 1956 Dr. Dick Read undertook a special trip to the Belgian Congo to study tribal practices in obstetric cases.

Prize Essays in Dermatology.—Dr. J. Graham Smith, of Miami, read his prize winning essay "The Aged Human Sebaceous Gland," at the 79th annual meeting of the American Dermatological Association, Inc., in June. Other prize winners in the annual contest were Dr. James H. Graham, of Philadelphia, and Dr. Elson B. Helwig, of Washington, D. C., "Bowen's Disease and Its Relationship to Systemic Cancer," second prize; Dr. Troy G. Rollins, of Woodland, Calif., "Necrobiosis Lipoidica Diabeticorum and Necrobiosis Lipoidica Granulomatosis," third prize; and Dr. Daphne Anderson Roe, of Wilmington, Del., "The Psoriatic Process," fourth prize. Papers for the 10th annual essay should be submitted to the Secretary, Dr. Wiley M. Sams, #308 Ingraham Building, Miami 32, Fla., not later than Nov. 15.

Announce Pediatric Award.—Applications are invited for a prize to be awarded by the Foundation Ernesto Cacace for Nepiology to the "best writer graduated from an Italian or foreign University or high institution of learning" on the subject, "Pathology and Medical Clinic of the Lactant Infant." The amount of the award will be 350,000 lire. Deadline for the presentation of the papers in six copies preferably in Italian is Dec. 31, 1961. Papers should be addressed to the Permanent Secretary of the Jury, Dr. Piero Repetto, Via Morghen 4, Turin, Italy. The award jury is composed of the foundation president and four members of the university staff. In the event this competition does not result in an award, the amount of the prize will be added to the funds of the foundation. Information may be obtained from Dr. Repetto.

Problems of the Crippled.—The 1959 annual convention of the National Society for Crippled Children and Adults, with sessions keyed to the theme "Searching Out Solutions," will be held in the Palmer House, Chicago, Nov. 29-Dec. 2. A training program for boards, volunteers, professional care, and treatment and administrative staffs of national, state, and local crippled children's societies, workshops will be devoted to "upgrading all facets of Easter Seal activity," according to Dr. Dean W. Roberts, executive director. The workshops will make case studies of problem areas with a view to developing solutions. The year 1959 marks the 38th anniversary of the National Society for Crippled Children and Adults. It has 1,655 Easter Seal affiliates in the 50 states, District of Columbia, and Puerto Rico, and aided almost 250,000 crippled children and adults in 1958.

Conference on Transmissible Animal Diseases.—The second annual Midwestern Interprofessional Conference on Diseases of Animals Transmissible to Man will be jointly sponsored by the State University of Iowa College of Medicine and the Iowa State Department of Health at Iowa City Sept. 10-11. The subjects will include brucellosis, rabies, leptospirosis, Q fever, staphylococcic diseases, and others. Presentations will be made by veterinarians and physicians and will emphasize the public health aspects and recent advances in these fields. This annual conference, the first of which was held at Omaha in 1958, will be held on a continuing annual basis sponsored in rotation by the academic institutes of the midwestern states. For information, write Dr. Ian Maclean Smith or R. A. Tjalma, D.V.M., State University of Iowa, University Hospitals—Department of Internal Medicine, Iowa City, Iowa, co-chairmen.

Summer Research Fellowships.—Summer research fellowships totaling $115,000 will be awarded this year to medical students in 97 U. S. and Canadian medical schools it has been announced by Lederle Laboratories Division, American Cyanamid Company. In a letter to medical schools, Dr. Benjamin W. Carey, Lederle medical director, stated that the medical student research fellowships are intended "to relieve in part the financial burden of students who desire to devote their summer vacations to research in the preclinical departments." Each four-year school receives $1,200 to be awarded to not less than two students, while each two-year college receives $600. Selections of the recipients of the fellowships are made by the deans of the medical schools. The Lederle fellowships have been given annually for six years. During this time almost $700,000 has been awarded to assist more than 1,000 medical students in this country, Puerto Rico, and Canada.

Mechanisms Concerned with Conception.—The Population Council, Inc., and the Planned Parenthood Federation of America, Inc., will present a conference, "Physiological Mechanisms Concerned with Conception," July 29-31, at the Hotel Thayer, West Point, New York. The conference will include the following topics:

Spermatogenesis and Sperm Physiology.
Physiology of Male Accessory Organs.
Ovogenesis and Ovulation.
Sperm Migration in the Female.
Fertilization and Implantation Mechanisms.
Immunological Phenomena.

The six sessions will be preceded by two days devoted to discussions in work groups. The final plenary session and dinner, 7:30 p. m., July 31, will include a summary of the conference. For information write Miss Margaret Snyder, Research Administrator, Planned Parenthood Federation of America, Inc., 501 Madison Avenue, New York 22.

Plan Nutrition Congress.—The fifth International Congress on Nutrition will be held in Washington, D. C., Sept. 1-7, 1960. Organized by the American Institute of Nutrition and the U. S. A. National Committee for Nutritional Sciences of the National Academy of Sciences, the congress is under the auspices of the International Union of Nutritional Sciences. Officers are: honorary president, Elmer V. McCollum, L.L.D., Baltimore; president, C. Glen King, Sc.D., New York City; chairman, organizing committee, Dr. Paul Gyorgy, Philadelphia; and general secretary, Milton O. Lee, Ph.D., Washington, D. C. The scientific program will consist of seven panel discussions, special programs on nine topics, an all-day symposium, "Food Needs and Food Resources," and 10-minute papers reporting original research. There will be scientific and industrial exhibits, visits to various scientific laboratories, a special program for women guests, and general entertainment activities for all registrants. For information, write: The Secretariat, Fifth International Congress on Nutrition, 9650 Wisconsin Ave., Washington 14, D. C.

Aero Medical Association Changes Name.—At the 30th annual meeting of the Aero Medical Association the society changed its name to the Aerospace Medical Association. Effective with the June number, the *Journal of Aviation Medicine* will be known as *Aerospace Medicine.* The 29th president of the association is Dr. Ludwig G. Lederer, of Washington. Dr. George J. Kidera, Chicago, was named president-elect, and Capt. Oran W. Chenault, Washington, D. C., was elected first vice-president. The association announced plans to establish a national headquarters in Washington, D. C., in the near future under the direction of Dr. William J. Kennard Jr., who was elected secretary-treasurer. He succeeded Dr. Thomas H. Sutherland, Marion, Ohio, who retired after holding that office since 1947. The Raymond F. Longacre Award was given to Capt. George E. Ruff Jr., Wright-Patterson Air Force Base, Ohio. The Arnold D. Tuttle Award was won by Dr. Lawrence E. Lamb, of the Air Force School of Aviation Medicine. Capt. Edward L. Beckman, on duty at the Royal Naval Institute of Aviation Medicine, Farnborough, England, was awarded the Eric Liljencrantz Medal. Capt. Clifford P. Phoebus, Newport, R. I., received the Theodore C. Lyster Award.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	June 20, 1959		June 21, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	2	3	2
New Jersey	..	..	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	3	..
Indiana	..	1	..
Illinois	..	2	1
Michigan	1	2	..
Wisconsin	1	1	..
West North Central States			
Minnesota	..	..	..
Iowa	11	17	..
Missouri	1	1	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	..
Kansas	1	2	1
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	..	..	2
West Virginia	..	1	1
North Carolina	4	4	3
South Carolina	..	..	1
Georgia	2	2	4
Florida	2	2	5
East South Central States			
Kentucky	2	2	1
Tennessee	1	1	..
Alabama	2	2	..
Mississippi	..	1	2
West South Central States			
Arkansas	6	7	..
Louisiana	4	4	2
Oklahoma	2	2	1
Texas	11	15	15
Mountain States			
Montana	..	..	..
Idaho	..	1	..
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	..	..	1
Arizona	1	1	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	4	1
Oregon	..	1	3
California	3	3	9
Alaska	..	..	..
Hawaii	..	..	7
Puerto Rico	..	..	..
Total	57	85	63

Conference on Mental Retardation.—The first International Medical Conference on Mental Retardation will be held July 27-31 at the Eastland Hotel, Portland, Maine. Papers to be presented by foreign participants include the following:

Developmental Anomalies in the Region of the Foramen Magnum, Dr. John D. Spillane, Cardiff, England.
Infections and Mental Deficiency, Dr. H. Asperger, Innsbruck, Austria.
Prenatal Infections, Dr. J. Sutter, Algiers, Algeria.
Dietary Treatment of Phenylketonuria—Experiences Over the Last Nine Years, Dr. H. Bickel, Marburg, Germany.
Lipid and Carbohydrate Metabolism and Mental Deficiency, Dr. P. B. Diezel, Heidelberg, Germany.
Copper, Iron and Lead Metabolism and the Brain, Dr. John N. Cumings, London, England.
Chemical Basis of Phenylketonuria, Dr. Cumings.
Etiological Aspects in Mongolism, Dr. J. Øster, Randers, Denmark.
Therapy in Mental Deficiency, Dr. Karl Kundratitiz, Vienna, Austria.
Chromosomal Factors in Some Types of Intellectual Subnormality, Dr. Paul E. Polani, London, England.
Behavior Problems in Brain Damaged Children, Dr. Asperger.

Scientific and commercial exhibits, a program of film exhibits, and social activities are planned. For information, write Dr. Ella Langer, State House, Augusta, Maine, Conference Secretary.

Report on Growth in Families.—American families continue to grow in number and size, it is reported by statisticians of the Metropolitan Life Insurance Company. There were about 38 million husband and wife families in the United States in March, 1958, a gain of 5.75 million, or 18%, during the past decade. In the same period, the number of families with three children under age 18 increased 68%, and those with four or more dependent children increased by 59%. Currently, the chances are 40 in 1,000 that a white father aged 25 will die before his newborn child reaches age 18. The likelihood of orphanhood rises rapidly with the age of the father at the time the child is born. The chances mount to 59 at age 30, to 93 at age 35, to 146 at age 40, to 221 at age 45, and to 323 at age 50. The chances that a newborn child will lose its mother are 15 in 1,000 in the mother is 20 when the child is born; then climb to 22 at age 25, to 33 at age 30, to 50 at age 35, to 76 at age 40, and to 115 at age 45. The Metropolitan statisticians point out that the American people are increasingly making provision to meet the contingency of premature death through life insurance, systematic saving, and other means. At the end of 1958, about 112 million policyholders in the United States owned nearly 500 billion dollars of life insurance in private companies.

Rhinologic Meeting in Chicago.—The American Rhinologic Society will hold its fifth annual meeting in the Belmont Hotel, Chicago, Oct. 10. This will be preceded by a surgical seminar in the Illinois Masonic Hospital, Chicago, Oct. 7-9. Dr. Kenneth

H. Hinderer, Pittsburgh, president of the society, will preside. The scientific program will include a "Symposium on Objective Tests for Nasal Function." Papers will include the following:

Trans-Septal Pituitary Extirpation, Dr. Walter E. Heck, San Francisco.
Choices of the Rhinologist in Approaching the Tear Sac, Dr. Lester T. Jones, Portland, Ore.
Surgery of Nasal Malignancies, Dr. John J. Conley, New York City.
Tissue Reactions to Nasal Transplants, Dr. William B. Barry, Kansas City, Mo.
Basic Immunology of Bone Transplants, Dr. James A. Dingwall, Squibb Institute for Medical Research, New Brunswick, N. J.

A showing of a film, "The Human Nose," will follow the evening dinner. Introductory remarks will be made by Dr. Richard B. Hadley, Rye, N. Y. Physicians and guests are invited. There is no registration fee. For information write Dr. Robert M. Hansen, secretary, 1735 N. Wheeler Ave., Portland 12, Ore.

Foreign Poliomyelitis Immunization Programs.—An immunization program with Wistar Institute attenuated live virus oral poliomyelitis vaccine is planned by the Polish public health authorities for a group of children in Poland. Dr. Hilary Koprowski, director of the Wistar Institute in Philadelphia and originator of its poliomyelitis vaccine, announced the program. Dr. Koprowski also made known how an oral immunization program with Wistar vaccine under the auspices of the Belgian Congo public health authorities was used to protect children in the Belgian Congo against a poliomyelitis epidemic late in 1958 and early in 1959. The Polish program, scheduled to begin in June, will administer strains of Wistar Institute live virus poliomyelitis vaccine to children from 6 months to 7 years who have not yet had a third injection of Salk-type vaccine. Adoption of the Wistar oral live virus vaccine stems from an investigation begun last December by the Polish State Institute of Hygiene. Dr. Felix Przesmycki, director of the Polish State Institute of Hygiene, spent several months at the Wistar Institute studying the production of the vaccine. Dr. Koprowski discussed the immunization project with the Polish public health authorities on two visits to Poland during the last 12 months. Belgian Congo public health authorities decided on immunization of children and infants with Wistar Institute live virus oral poliomyelitis vaccine because their records indicated an increasing incidence of poliomyelitis in the Congo from 1951 through 1957. The program for Leopoldville now under way calls for immunization of 75,000 children between the ages of 6 months and 5 years with Type I Wistar Institute oral vaccine. Immunization in Leopoldville has proceeded at a rate of about 8,000 children a month, both native and European.

CANADA

Install Duke of Edinburgh as President.—The installation of His Royal Highness, Prince Philip, Duke of Edinburgh, as president of the Canadian Medical Association was held in Toronto Tuesday, June 30. Dr. Arthur D. Kelly, general secretary of the association said that His Royal Highness will not be accepting the presidency as an honorary appointment. "He will actually be our President for the ensuing year," said Dr. Kelly. "The event will be of historic interest, as this will be the first time that a nonmedical person has been appointed President of the C. M. A." Dr. Kelly also stated that the many duties of the office will be carried out by Dr. E. Kirk Lyon, of Leamington, Ontario, who has been elected Canadian Deputy to the President. Special guests at this ceremonial meeting of installation were Sir Arthur Thomson, of Birmingham, president, British Medical Association; Dr. Louis M. Orr, of Orlando, Fla., President, American Medical Association; and Dr. Emil Blain, of Montreal, president of l'Association des Médecins de Langue Française du Canada.

FOREIGN

Congress on Therapeutics.—The sixth International Congress on Therapeutics will be held Oct. 1-3 at the Palace of the University of Strasbourg, France. Three congress subjects have been chosen by the international committee: (1) the damages of abusive gastrectomies for gastroduodenal ulcer, (2) anti-inflammatory medications, and (3) antitussive medicines. A medical exposition is planned. Prof. R. Fontaine, dean of the Faculty of Medicine, University of Strasburg, is president of the congress, and Prof. F. Schmid, professor of pharmacology at the university, is the general secretary.

Meeting on Voice and Speech in London.—The 11th International Congress of Logopedics and Phoniatrics will be held Aug. 17-22, at the Kings College, London. Two symposiums are planned: "Common Traits in Normal Language Development, Dyslalia, Dyslexia and Aphasia," and "Pathologie der Resonanzraume bei Gaumenspalten." The program will include participants from the Netherlands, Spain, Hungary, Czechoslovakia, France, Sweden, Germany, Poland, Australia, the United States, and England. For information write Miss Peggy Carter, 46 Canonbury Square, London, N. 1, England, secretary of the congress.

Medical Congress in South Africa.—The Medical Association of South Africa will hold its 42nd medical congress Sept. 27-Oct. 3 in East London, Cape Province, under the presidency of Dr. P. F. Wagner. Three symposiums are planned for the plenary sessions on cancer, heart disease, and tuberculosis. Congress visitors will include the following: Sir Russell Brock, London; Dr. George E. Burch, New

Orleans; Prof. Robert McWhirter, Edinburgh, Scotland; Dr. Harold Stewart, Bethesda, Md.; Dr. A. Ravin, Denver; Dr. Rose Ravin, Denver; and Dr. Rex L. Diveley, Kansas City, Mo. A trades exhibition, a scientific exhibition, and an arts and hobbies exhibition are planned. A ladies' program and a program of sports and entertainment are arranged. For information, write Dr. E. McCabe, Honorary Organizing Secretary, Medical Congress Office, Third Floor, Ensuco House, 10-12 Oxford St., East London, South Africa.

Symposium on Depression.—The University of Cambridge, England, will hold a symposium on depression Sept. 22-26. The symposium will consist of lectures and discussions on the following aspects of the subject: (1) clinical, (2) neuro-pharmacological, (3) psychological, and (4) therapeutic. Lectures will be given during the morning with discussion by group in the afternoon. The aim of the symposium is to describe the growth of opinion and to give current views on the nature of depression and its treatment. The symposium, primarily intended for those engaged in the practice of psychiatry and for university research or teaching staffs, will be introduced by Prof. Aubrey Lewis, of London. Fee for the course is £6 6s. 0d.; part-time attendance is at the rate of £1 11s. 6d. per day. The proceedings will be in English and will be published by the Cambridge University Press. Registration forms may be obtained from the Secretary of the Medical School, Tennis Court Road, Cambridge, England.

CORRECTIONS

Highlights of Atlantic City Meeting.—In the section entitled Related Activities in Highlights of Atlantic City Meeting (June 27 issue, page 1076) the third line of the paragraph beginning "Meeting at the . . ." should follow the third line of the paragraph beginning "America's younger generation. . . ."

The Management of Cardiac Arrest.—In the article by Davis and associates in the June 27 issue on page 1051, the second sentence of the paragraph beginning "The thoracic cavity. . . ." should begin "One million units of penicillin . . ." instead of "One million cubic centimeters of penicillin. . . ."

President Coolidge Also Addressed the A. M. A.—The Journal, June 27, page 1072, stated that President Eisenhower's address before the Annual Meeting of the American Medical Association in Atlantic City, June 9, was the first time that the Association had been honored by the participation of the President of the United States in its program. The Journal now finds that President Calvin Coolidge addressed the opening meeting of the American Medical Association Tuesday, May 17, 1927, during the Annual Meeting of the Association in Washington, D. C.

Amphetamine Sulfate and Athletic Performance.—The study by Gene M. Smith, Ph.D., and Henry K. Beecher, M.D., in The Journal of May 30, 1959, page 542, was completed only a short time before publication. Development of the report and arrangements for printing it concurrently with public announcement of the recommendations of the American Medical Association's Special Committee on Amphetamines and Athletes were, therefore, necessarily hurried. For this reason some errors appeared in the paper. The authors did not receive proofs and had no opportunity to correct them before publication. Corrections have been made in the author's reprints. The essential corrections are as follows.

The Tables.—The data reported in table 2 were transposed in a typesetting error. The results reported under the heading "First Swim, Rested Condition" should have been presented under "Second Swim, Fatigued Condition" and vice versa. In the body of that same table the symbol $\overline{P}\text{-}\overline{A}$ should be $\overline{\overline{P}\text{-}\overline{A}}$ and the symbol $\frac{\overline{P}\text{-}\overline{A}}{\overline{P}}$,% should be $\frac{\overline{\overline{P}\text{-}\overline{A}}}{\overline{P}}$,%. The first note in the legend should read: $\overline{\overline{P}\text{-}\overline{A}}$ = mean difference for the group of $\overline{P}\text{-}\overline{A}$ scores presented in table 1. The second note should read: $\overline{\frac{\overline{\overline{P}\text{-}\overline{A}}}{\overline{P}}}$,% = mean difference . . . instead of: $\frac{\overline{P}\text{-}\overline{A}}{\overline{P}}$,% = mean difference . . .

Similar errors in symbol notation occurred in other tables, but if the tables are examined in relation to the text, they are understandable. Table 3 contains two numerical errors. Under the heading: "Swimming in competition, 3 Hr. After Medication," the p value fifth from the bottom should be 0.02 rather than 0.20. In the third column from the right the value −0.30 should read −0.39. In table 14, the second column from the right reports the value of −0.31. The sign should have been plus rather than minus. The tables in the author's reprints have the correct symbols and numerical values.

Errors in the Text.—The section on Medicaments (pages 542 and 543) may be misleading. The point to be clarified is this: Each subject participating in a given experiment was studied under all types of medication used in that experiment and was studied under each agent several (three on the average) times.

On page 545, in the first paragraph under Method, *Experiment 3*, the sixth sentence reads: "The subjects were given 14 mg. of amphetamine per 70 kg. on two occasions, with 50 mg. of secobarbital per 70 kg. on two and with placebo on two." The word "with" should have been deleted both times in that sentence. The point to be clarified is this: No subject took both amphetamine and secobarbital on the same day.

On page 550 under Results, *Experiment 1*, the seventh paragraph begins: "Table 1 . . ." It should read: "Table 2 . . ." In that same paragraph the following material should have been deleted:

"(mean placebo minus mean amphetamine/mean placebo)." In the tenth paragraph of that same section the sentence beginning, "The 10-yd. men . . ." should read, "The 100-yd. men . . ."

On page 552, under Results, *Experiment 4*, in the second paragraph the word "variable" should be plural and the word "date" should be data."

On page 553, under Results, *Experiments 2, 3, and 4 Combined*, the word "man" in the second sentence should be "mean." In the second paragraph of that same section the following symbols should have been deleted: $(\overline{P}\text{-}\overline{A}/\overline{P}\%)$.

On page 554, under Results, *Experiment 6*, the first paragraph has a sentence reading as follows: "The total group 't' yields a mean difference of 0.63 second, of 2.14 which is significant beyond the 0.05 level." That sentence should read: The total group mean difference of 0.63 second yields a 't' of 2.14 which is significant beyond the 0.05 level." The last sentence in that same paragraph is also in error. It should read: "The 't' value for the 0.64% improvement shown by the total group was 2.49, with a corresponding two-tailed probability value beyond the 0.05 level."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *1959 Schedule—Written*, Oct. 19. Final date for filing application was May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certificates, new and reopened, Part I, and requests for re-examination Part II are now being accepted. *Part I. Written.* Jan. 15, 1960. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1959. No applications can be accepted after that date. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-9. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: New Orleans, Nov. 12-14. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PATHOLOGY: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, September. Final date for filing application was March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Chicago, Oct. 19-20; New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Examination.* Washington, Dec. 6-9. Deadline for filing application is July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country, September 1959. Final date for filing application was July 1. *Oral.* September. Final date for filing application was July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

AMERICAN BOARD OF UROLOGY: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

ARMY

Personal.—Col. John W. Raulston, former deputy commander of Brooke Army Hospital, has taken command of the 67th Medical Group, and Col. John H. Taber has moved to the post of hospital deputy commander.

NAVY

Personal.—Rear Adm. Bruce E. Bradley, M. C., who has been deputy and assistant chief of the Bureau of Medicine and Surgery for the past four years, became commanding officer of the National Naval Medical Center, Bethesda, Md., in June. Rear Adm. Edward C. Kenney, M. C., is the new deputy and assistant chief of the bureau. At the Medical Center, Admiral Bradley will relieve Rear Adm. Thomas F. Cooper, M. C., who has retired.—–Rear Adm. Bartholomew W. Hogan, the surgeon general of the Navy, was appointed North American chairman of the Pan American Medical Association's section on military medicine.—–Capt. Donald R. Childs, M. C., was assigned to the Bureau of Medicine and Surgery as director of the publications division.—–Capt. Kenneth P. Bachman, M. C., retired after more than 16 years of active duty.—–Capt. George M. Bell, M. C., retired after 18 years of active duty.—–Capt. John H. Cox, M. C., retired after more than 19 years of active duty.

PUBLIC HEALTH SERVICE

Personal.—Dr. Floyd S. Daft, director of the National Institute of Arthritis and Metabolic Diseases, was named president-elect of the American Institute of Nutrition. He will succeed to the presidency on July 1, 1960. The American Institute of Nutrition is one of six scientific organizations comprising the Federation of American Societies for Experimental Biology.—–Dr. John C. Whitehorn, Henry Phipps professor and director of the department of psychiatry at the Johns Hopkins University School of Medicine, was appointed to the National Advisory Mental Health Council. He also served on the council from 1954 to 1958.—–Dr. John S. Lawrence, professor and chairman of the department of medicine at the University of California, Los Angeles, was appointed to the National Arthritis and Metabolic Diseases Council and will serve through Sept. 30, 1963.

Poliomyelitis.—Almost twice as many cases of paralytic poliomyelitis were reported in the first four months of 1959 as in the same period in 1958. Because a 45% increase in paralytic cases also occurred in 1958 over 1957, the surgeon general urged a renewed vaccination effort. In the first week of May, 19 new cases were reported as compared to only 7 for the same week in 1958. A total of 283 cases has been reported so far in 1959 compared with 147 for the same period last year. Vaccine shipments to fill domestic orders totaled 2,300,000 doses for the last week of April, a record high for 1959, indicating some increase in the numbers being vaccinated, but it is estimated that at least 50 million persons in the high risk group—those under 40 years of age—have not been fully vaccinated.

Insecticidal Fumes.—Willis Mathis and co-workers at the Savannah, Ga., laboratories of the Communicable Disease Center discovered what may prove to be an important new method of killing household mosquitoes. An unopened bag of insecticide was left inside a large laboratory where adult mosquitoes were confined for testing. Overnight, most of the mosquitoes died. Suspecting that fumes from the closed bag were responsible, the scientists decided to experiment. Their theory was confirmed. They found that the fumes killed mosquitoes even when the insecticide was enclosed in a paper bag with a polyethylene liner. In repeated experiments, the method worked even in rooms that were well ventilated. The most effective of the chemicals tested were malathion and DDVP, used in combination or separately. Both chemicals have been widely used against mosquitoes in recent years. More study will be required and specific techniques worked out before the method may be generally applied. Although the insecticides used are known to be relatively safe for human beings, further experiments must be conducted to determine that all possible human hazards are eliminated, but once the technique has been perfected and proved safe, it may greatly simplify control of mosquitoes.

Poliomyelitis Vaccine.—A committee of advisors reviewed the experience to date with the Salk poliomyelitis vaccine and concluded that groups vaccinated with the recommended series of three doses of vaccine have maintained a high degree of protection against poliomyelitis. Vaccine has been available to the public since 1955, and groups vaccinated over three years ago still maintain an appreciable protection against the disease. Studies of patients who had poliomyelitis in 1958 indicate that the probability of contracting the paralytic form has been reduced about 75% for those who had received the basic series of three injections of vaccine as compared with nonvaccinated persons. In some groups of children the probability of contracting the paralytic form has been reduced about 90% for those who had received the full basic course of three doses of poliomyelitis vaccine as compared to nonvaccinated children of the same age. Cases of paralytic poliomyelitis have occurred in persons who have received the basic course of injections of vaccine, but most cases of paralytic poliomyelitis occurring in 1958 were among unvaccinated persons.

In the light of present knowledge and experience the surgeon general's committee of advisors presents the following recommendations for poliomyelitis vaccination:

1. Completion of the basic series of three injections of Salk type vaccine is recommended for all persons under 40 years of age who have not yet been vaccinated or who have received fewer than three doses of vaccine. Vaccination of persons aged 40 and over can also be beneficial, but it is less urgent since poliomyelitis occurs less frequently in older persons. The recommended basic schedule for all persons, except young infants, is three doses of 1 ml. each as follows: an initial injection, a second injection four to six weeks after the first, and a third injection 7 to 12 months after the second dose.

2. A basic schedule of four injections, recommended for infants less than 6 months of age, consists of a series of three injections of 1 ml. each of the vaccine, spaced one month apart beginning before 6 months of age and as early as 2 months of age, followed by a fourth injection 7 to 12 months after the third dose. Poliomyelitis vaccine for infants and young children may be given as separate injections or in quadruple vaccines which combine poliomyelitis vaccine with diphtheria, pertussis, and tetanus vaccine. The schedule recommended by the manufacturer of such quadruple vaccines can be followed when this product is used. Infants under 6 months of age do not always develop an adequate antibody response from two initial injections so that the third primary injection appears desirable. Vaccination early in infancy is recommended, but complete information on optimal dosage schedules will require further experience with the separate and quadruple vaccines.

3. It is recommended that a booster dose of 1 ml. of poliomyelitis vaccine be given to persons under 40 years of age who have completed the basic series of three doses at least one year previously and especially if several years have elapsed since completion of the basic series of injections. Such a booster dose is expected to increase antibody titers in persons in whom the antibody levels have fallen or in whom the initial antibody response was weak, thereby providing possible added protection against poliomyelitis.

4. A booster dose of 1 ml. of poliomyelitis vaccine for vaccinated persons is especially indicated for persons entering situations or traveling into areas where the incidence of poliomyelitis is high, for example, (*a*) at the beginning of local epidemics of poliomyelitis—emergency booster doses as early as one month after the previous dose of vaccine, regardless of the number of previous doses; (*b*) when preschool children are to enter school; (*c*) for pregnant women prior to the poliomyelitis season—for the vaccine not only provides added protection against the disease for the mother but also provides a passive immunity to the unborn baby; and (*d*) for persons traveling into areas where sanitation may be poor or poliomyelitis is known to be present.

These recommendations have been drawn up with the advice of Col. Donald M. Alderson, U. S. A. F., M. C., assistant for professional services, office of the assistant secretary of defense (health and medical); Dr. Gordon Brown, professor of epidemiology, University of Michigan School of Public Health; Lt. Col. Joseph W. Cooch, chief, Communicable Disease Branch, Department of the Army; Dr. Edward C. Curnen, chairman, Committee on the Control of Infectious Diseases, American Academy of Pediatrics; Dr. Geoffrey Edsall, chairman, Committee on Immunization of the Armed Forces Epidemiology Board; Dr. Hollis S. Ingraham, first deputy commissioner, New York State Health Department; Dr. Cyrus Maxwell, Washington Medical Liaison, American Medical Association; Dr. Andrew C. Offutt, Indiana health commissioner, Dr. James C. Overall, president of the American Academy of Pediatrics; Dr. Julian P. Price, Chairman of the Poliomyelitis Committee of the American Medical Association; Dr. Thomas M. Rivers, vice-president–medical affairs, the National Foundation; Dr. Jonas Salk, professor of experimental medicine and director of Virus Research Laboratory, School of Medicine, University of Pittsburgh; and a number of officials from the Public Health Service.

ARMED FORCES INSTITUTE OF PATHOLOGY

New Scientific Director.—Robert E. Stowell, M.D., has been appointed scientific director of the Institute of Pathology He succeeds Ernest W. Goodpasture who resigned in April. Dr. Stowell comes to the Institute from the University of Kansas Medical Center, Kansas City, Kan., where for the past 11 years he was professor and chairman of the department of pathology and oncology and the director of cancer research.

FOOD AND DRUG ADMINISTRATION

Personal.—Dr. William H. Kessenich was named medical director of the Food and Drug Administration in June. He has been acting medical director since January, when Dr. Albert H. Holland Jr., the former director, resigned.

DEATHS

Alcorn, James Garfield Ⓜ Columbus, Ohio; Miami Medical College, Cincinnati, 1902; on the staff of the Grant Hospital; died April 29, aged 78.

Anderson, Laurence Engel Ⓜ Greentown, Ohio; Ohio State University College of Medicine, Columbus, 1929; member of the American Academy of General Practice; interned at St. Luke's Hospital in Cleveland; served as president, secretary, and treasurer of the Stark County Medical Society; member and past-president of the staff at Aultman Hospital in Canton; on the courtesy staff, Mercy Hospital in Canton; died April 26, aged 57.

Applegate, Frederick Martin, Monahans, Texas; Indiana University School of Medicine, Indianapolis, 1929; veteran of World War II; died in the Ward Memorial Hospital April 17, aged 55.

Ashworth, Adrian Lincoln Ⓜ Buckhannon, W. Va.; Rush Medical College, Chicago, 1937; interned at the Swedish Covenant Hospital in Chicago; served a residency at the Weston (W. Va.) State Hospital; veteran of World War II; on the staff of the Elizabeth Coplin Leonard Hospital, where he died May 2, aged 49.

Bernstein, Clarence Ⓜ Orlando, Fla.; born in Nashville, Tenn., July 19, 1905; Johns Hopkins University School of Medicine, Baltimore, 1931; from 1928 to 1932 engaged in special investigative work in pathology and immunology at his alma mater, receiving the Mellon Research Fellowship for the year 1931-1932; house officer on the Harvard Medical Service at Boston City Hospital, 1932-1933; while practicing in Chicago, was assistant in the department of medicine from 1933 to 1935 at the University of Chicago, served on the staffs of the Michael Reese Hospital and Cook County Hospital, was consultant in medicine for the Institute of Psychoanalysis of Chicago, and was a member of the teaching staff at Northwestern University Medical School; specialist certified by the American Board of Internal Medicine; secretary, session on allergy, Section on Miscellaneous Topics, American Medical Association, in 1957; a member and past-president of the Southeastern Allergy Association; a founder and past-president of the Florida Allergy Society; an honorary member of the Allergy Society of Cuba; fellow of the American Academy of Allergy and from 1955 to 1958 on its executive committee; fellow of the American College of Allergists; member of the Central Society for Clinical Research, American Psychosomatic Society, American Association for the Advancement of Science, World Medical Association, and Federation of American Scientists; a member of the Phi Beta Kappa, Sigma Xi, and the Alpha Omega Alpha, honorary medical fraternity; since 1942 medical advisor of the U. S. Selective Service System; a staff member of the Orange Memorial Hospital, Florida Sanitarium and Hospital, and the Winter Park (Fla.) Memorial Hospital; one of the founders of the Central Florida Symphony Association and served on its board of directors; died April 23, aged 53.

Bishop, Linton Hines Sr., Unadilla, Ga.; Atlanta College of Physicians and Surgeons, 1908; chairman of the school board; died in the Crawford W. Long Memorial Hospital, Atlanta, April 19, aged 77.

Blake, Austin M., Waunakee, Wis.; Eclectic Medical Institute, Cincinnati, 1887; a founder and director of the Waunakee State Bank; died April 19, aged 95.

Blake, Margaret Adler, Perry Point, Md.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1951; certified by the National Board of Medical Examiners; interned at the Queens General Hospital in New York City; served a residency at the New York City Hospital and Veterans Administration Hospital in Albuquerque, N. Mex.; associated with the Veterans Administration Hospital in Perry Point; died in the Memorial Hospital April 24, aged 32.

Blankenship, Joseph Charles, Sparta, Tenn.; University of Tennessee College of Medicine, Memphis, 1916; veteran of World War I; formerly vice-superintendent of the Davidson County Hospital and Home in Nashville; died in the White County Hospital April 19, aged 71.

Blanton, Harvey Chenault Ⓜ Richmond, Ky.; University of Louisville (Ky.) School of Medicine, 1936; interned at the Charity Hospital in New Orleans; veteran of World War II; past-president of the Madison County Medical Society; on the staff of the Pattie A. Clay Infirmary; died April 19, aged 47.

Bloom, Charles Francis Ⓜ Bremerton, Wash.; University of Oregon Medical School, Portland, 1915; for many years associated with the Veterans Administration in various cities, retiring Sept. 30, 1949; served as a member of the Arkansas State Board of Medical Examiners; died in the Harrison Memorial Hospital April 12, aged 78.

Ⓜ Indicates Member of the American Medical Association.

Bojars, Kazimirs, Chicago; Latvijas Universitäte Medicinas Fakultate, Riga, Latvia, 1940; died April 22, aged 56.

Boyd, Harry Wilson, Los Angeles; University of Pennsylvania Department of Medicine, Philadelphia, 1899; served as a medical missionary in China; died April 22, aged 87.

Bradley, John William Ⓜ Chattanooga, Tenn.; Atlanta Medical College, 1915; veteran of World War I; died May 1, aged 65.

Brickner, Richard Max Ⓜ New York City; born in New York City Nov. 20, 1896; Columbia University College of Physicians and Surgeons, New York City, 1923; assistant clinical professor of neurology at his alma mater; fellow in pathology at the National Research Council, 1925-1926; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War I; during World War II consultant to the Selective Service System and was awarded the Selective Service Medal by United States Congress; vice-chairman, Section on Nervous and Mental Diseases, American Medical Association, 1938-1939; member of the Harvey Cushing Society, American Neurological Association, American Psychosomatic Society, American Psychiatric Association, and the Association for Research in Nervous and Mental Diseases; fellow of the American Association for the Advancement of Science; past-president of the New York Neurological Society; a founder and honorary fellow of the National Multiple Sclerosis Society; author of "Intellectual Functions of the Frontal Lobe"; for many years on the staffs of the Neurological Institute of the Columbia–Presbyterian Medical Center and Mount Sinai Hospital, where he died April 25, aged 62.

Burge, Aaron D. Ⓜ Warren, Ind.; Eclectic Medical Institute, Cincinnati, 1897; died in the Methodist Memorial Home Hospital April 25, aged 87.

Burley, David Henry Ⓜ Almont, Mich.; Detroit College of Medicine, 1893; village health officer; also a registered pharmacist; active in organizing the new Community Hospital, where he was an honorary member of the staff; in 1953 "Doctor Burley Week" was celebrated in honor of his 60 years of practice and at that time he was awarded with a special citation for outstanding service and honor brought to the medical profession; died April 20, aged 95.

Byers, Norman Roy, Bedford, Ind.; Indiana University School of Medicine, Indianapolis, 1919; veteran of World War I; past-president of the Kiwanis Club; died March 9, aged 64.

Callahan, Timothy Andrew Jr., Mosquero, N. M.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1938; veteran of World War II; died May 3, aged 44.

Campbell, Alexander W., Elkton, Mich.; Saginaw Valley Medical College, Saginaw, 1903; died in the Hubbard Memorial Hospital, Bade Axe, April 19, aged 81.

Casson, Paul William Ⓜ New York City; Fordham University School of Medicine, New York City, 1921; died March 21, aged 62.

Coffin, Lonnie Alfonso Ⓜ Farmington, Iowa; born June 13, 1890; Drake University of Iowa College of Medicine, Des Moines, 1913; member of the American Academy of General Practice and the Iowa Academy of General Practice; past-president and served on the board of trustees of the Iowa State Medical Society and in April, 1958, was named "Iowa Outstanding General Practitioner of the Year"; on Dec. 2, 1958, at Minneapolis was honored by the American Medical Association as the "General Practitioner of the Year"; veteran of World War I; for many years served on the school board and for four years on the town council; associated with the Graham Hospital in Keokuk, where he died April 28, aged 68.

Cohn, Hans Joachim Ⓜ Woodstock, N. Y.; Ernst–Moritz–Arndt Universität Greifswald Medizinische Fakultät, Greifswald, Prussia, 1932; a veteran of World War II, served as a paratrooper with the 11th Airborne Division and was the recipient of the Silver Star for gallantry in action in 1944 on Leyte; also received the Medical Combat Badge and four battle stars; associated with the Kingston Hospital and Benedictine Hospital in Kingston; died April 18, aged 52.

Coleman, James Emory, Fayetteville, W. Va.; Kentucky School of Medicine, Louisville, 1894; fellow of the American College of Surgeons; served as health officer of Fayette County; died April 29, aged 91.

Connor, John Joseph Ⓜ St. Louis; St. Louis University School of Medicine, 1922; for many years St. Louis County coroner; senior instructor in surgery at his alma mater; on the staff of St. Mary's Group of Hospitals; died in St. Mary's Hospital April 28, aged 65.

Cornish, Solon Washington, Everett, Mass.; Harvard Medical School, Boston, 1909; served on the staff of the Whidden Memorial Hospital; died April 20, aged 76.

Corr, Francis Xavier, Boston; Boston University School of Medicine, 1898; served as a member of the state board of registration in medicine; a staff physician at Boston State Hospital; died in the Boston City Hospital April 15, aged 93.

Cosgrove, Louie Cooper Sr. Ⓜ Swanton, Ohio; Toledo Medical College, 1901; served as Fulton County coroner for two terms and was formerly Swanton mayor and village councilman; past-president of the school board of Swanton; served with the American Expeditionary Force overseas during World War I; died in St. Vincent's Hospital, Toledo, April 21, aged 79.

Crampton, Harrison Frank, Coraopolis, Pa.; Howard University College of Medicine, Washington, D. C., 1937; veteran of World War II; died in the Elizabeth Steel Magee Hospital in Pittsburgh April 18, aged 48.

Cronheim, Irma Klausner Ⓜ Oceanside, N. Y.; Martin Luther Universität Medizinische Fakultät, Halle-Wittenberg, Prussia, 1901; member of the American Psychiatric Association; served as resident physician at the Oceanside Gardens Sanitarium; died April 24, aged 85.

Davies, Leroy William, Bismarck, Mo.; National University of Arts and Sciences Medical Department, St. Louis, 1918; died April 15, aged 71.

Davis, Samuel Jones Tilden, Raytown, Mo.; University Medical College of Kansas City, 1905; president of the Raytown Water Company; for many years practiced in Kansas City; died April 21, aged 82.

Dew, Thomas Welch Ⓜ Fredericksburg, Va.; Medical College of Virginia, Richmond, 1893; president one term of the Medical College of Virginia Alumni Association; on the staff of the Mary Washington Hospital; died April 27, aged 88.

Edison, Samuel Martin, Miami Beach, Fla.; College of Physicians of Chicago, School of Medicine of the University of Illinois, 1906; veteran of World War I; formerly practiced in Chicago, where he was associated with Michael Reese and Augustana hospitals; died in the Veterans Administration Hospital in Coral Gables April 11, aged 74.

Enkelis, Jacob J. Ⓜ Portland, Ore.; University of Oregon Medical School, Portland, 1926; veteran of World War II; interned at New Haven (Conn.) Hospital; served a residency at Mount Sinai Hospital in New York City; on the staff of the St. Vincent's Hospital and the Good Samaritan Hospital, where he was president of the medical staff in 1956-1957, and where he died April 17, aged 59.

Fisher, Nelson Franklin Ⓜ Chicago; Rush Medical College, Chicago, 1927; certified by the National Board of Medical Examiners; veteran of World War I; served on the staff of St. Luke's Hospital; for a number of years a member of the board of trustees of the Gettysburg (Pa.) College; died in the Veterans Administration Research Hospital April 25, aged 63.

Fleetwood, Doyle Homer Ⓜ Edmond, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1941; member of the American Academy of General Practice; in 1947 founded the Edmond Hospital which he operated until his retirement; a member of the Kiwanis Club for many years and served several terms on the board of directors of the local chamber of commerce; died in the Oklahoma Medical Research Hospital, Oklahoma City, April 14, aged 55.

Flood, William Arthur, North Bennington, Vt.; University of Vermont College of Medicine, Burlington, 1911; veteran of World Wars I and II; joined the staff of the Veterans Administration and served in hospitals throughout the country until his retirement on March 31, 1951; during World War II served as assistant director of the Veterans Administration Hospital in Lyons, N. Y.; died in the Veterans Administration Hospital, Albany, April 11, aged 71.

Flynn, Southard Tolchard Ⓜ Flint, Mich.; University of Michigan Medical School, Ann Arbor, 1926; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; veteran of World War II; president of the Flint Academy of Surgery; associated with Hurley, McLaren General, and St. Joseph hospitals; died April 21, aged 61.

Fox, Joseph Andrew, Hinton, W. Va.; University of Nashville (Tenn.) Medical Department, 1903; served as county coroner; died in a hospital at Weston April 24, aged 84.

Frame, Joseph Harlan Ⓜ Wilmington, Ohio; Starling-Ohio Medical College, Columbus, 1909; past-president of the Clinton County Medical Society; on the staffs of the Miami Valley Hospital in Dayton, Fayette County Memorial Hospital, Washington Court House, Our Lady of Mercy Hospital in Mariemont, and the Clinton Memorial Hospital; died in the Christian R. Holmes Hospital in Cincinnati April 13, aged 77.

Franke, Fred C., Oak Park, Ill.; (licensed in Illinois in 1898); served on the staff of St. Anthony de Padua Hospital in Chicago; died in the U. S. Public Health Service Hospital, Chicago, April 22, aged 85.

Franklin, John Thomas Wilson, Detroit; Meharry Medical College, Nashville, Tenn., 1941; veteran of World War II; died April 9, aged 41.

Freedman, Barnett Philip Ⓜ New Haven, Conn.; Yale University School of Medicine, New Haven, 1920; past-president of the Connecticut Society of Allergy; consultant allergist at Grace–New Haven Hospital; served on the staff of the Jewish Hospital in Brooklyn; died in Woodbridge April 14, aged 62.

Fry, Howard Leslie, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1907; died April 14, aged 74.

Fudell, Joseph Erwin Ⓜ Brooklyn; St. Louis University School of Medicine, 1932; on the staff of the Brooklyn Women's Hospital and the Lefferts General Hospital, where he died March 5, aged 51.

Giering, Charles Noble Ⓜ Midland, Mich.; Western Reserve University School of Medicine, Cleveland, 1950; served an internship and residency at the Youngstown (Ohio) Hospital; specialist certified by the American Board of Anesthesiology, Inc.; member of the American Society of Anesthesiologists, Inc.; on the staff of the Midland Hospital; veteran of World War II; died April 20, aged 36.

Gillespie, David Halliday Moffat Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1902; fellow of the American College of Surgeons; consulting surgeon at the Grand Central Terminal; consulting surgeon and served as dean of the surgical services at the Hospital for Ruptured and Crippled, now known as Hospital for Special Surgery; died in the Midtown Hospital Feb. 27, aged 84.

Gordon, Frank Scott Ⓜ Blairstown, N. J.; New York University Medical College, New York City, 1898; medical examiner of the Blairstown schools for 40 years; devoted most of his spare time to literature and art; his paintings were exhibited at various galleries and he received several awards and plaques for his work; died April 23, aged 82.

Haggard, Howard Wilcox, New Haven, Conn.; born in La Porte, Ind., July 19, 1891; Yale University School of Medicine, New Haven, 1917; captain in the chemical warfare service, U. S. Army, 1917-1918; consulting physiologist for the U. S. Bureau of Mines from 1919 to 1922; instructor of physiology at his alma mater from 1919 to 1923 and assistant professor from 1923 to 1926; associate professor of applied physiology, Sheffield Scientific School at Yale, from 1926 to 1938; for many years professor, and director of Laboratory of Applied Physiology at Yale; founder of the Center of Alcohol Studies at Yale University; instrumental in organizing the Summer School of Alcohol Studies at Yale and was also instrumental in establishing the Yale Plan Clinic, which set a nation-wide pattern for scientific work with alcoholics; from 1948 to 1950 served as director of the Yale Office of University Development, during which period he toured the country twice, visiting practically every Yale Club of alumni in the nation; physiologist for the New York and New Jersey Tunnel Commission; member of the Third Resuscitation Commission; member of the American Society of Biological Chemists, American Physiological Society, International Anesthesia Society, American Social Hygiene Association, Connecticut Academy of Arts and Sciences, Nu Sigma Nu, Phi Sigma Kappa, and Sigma Psi; editor of the *Quarterly Journal of Alcohol Studies,* a post held since the journal was established in 1940; was the author of numerous publications, both professional and popular, including "Devils, Drugs and Doctors," "The Lame, the Halt, and the Blind," "Staying Young Beyond Your Years," and "Alcohol Explored"; died in Fort Lauderdale, Fla., April 22, aged 67.

Hall, John Baptiste Sr. Ⓜ Chicago; University of Pennsylvania Department of Medicine, Philadelphia, 1901; formerly practiced in Boston and at one time appointed to the advisory council of the state department of public health; served as medical examiner for the Massachusetts Insurance Department and as a medical inspector for the Boston schools; died in the Chicago Home for Incurables April 23, aged 82.

Harris, Charles Houston II Ⓜ Fort Worth, Texas; University of Texas School of Medicine, Galveston, 1942; interned at Harris Memorial Methodist Hospital in Fort Worth and served a residency at Scott and White Hospital in Temple; veteran of World War II; fellow of the American College of Surgeons; on the staff of the Harris Hospital; vice-chairman of the board, Harris College of Nursing at Texas Christian University, where he was university physician; died in Baylor University Hospital, Dallas, April 21, aged 44.

Hart, John Thomas Ⓜ Chicago; University of Tennessee College of Medicine, Memphis, 1923; fellow of the American College of Surgeons; veteran of World War I; on the staffs of the Alexian Brothers and Grant hospitals; died in the Henrotin Hospital April 30, aged 64.

Hathcock, Alfred Lawrence Ⓜ Palestine, Texas; University of Pennsylvania Department of Medicine, Philadelphia, 1892; past-president of the Texas Surgical Society; fellow of the American College of Surgeons; died May 2, aged 92.

Heidrick, Daniel Lawrence Ⓜ Mercedes, Texas; University of Kansas School of Medicine, Kansas City, 1906; served as mayor; veteran of World War I; died April 13, aged 75.

Hempstead, Bert Eugene Ⓜ *Rochester, Minn.; born* in Bloomington, Ill., Jan. 28, 1884; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; served an internship at the Northern Pacific Beneficial Association Hospital in Brainerd; at one time practiced in Duluth, Minn., and Miles City, Mont.; a member of the Mayo Clinic from 1921 until his retirement in 1950; in 1918 came to the clinic as a first assistant in the section of otolaryngology and rhinology and was appointed to the staff in 1921; successively instructor, assistant and associate professor in the Mayo Foundation, Graduate School of the University of Minnesota; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, the Alumni Association of the Mayo Foundation, and the Society of the Sigma Xi; on the staffs of the Methodist Hospital and St. Mary's Hospital, where he died April 16, aged 75.

Henely, Edmund, Osage, Iowa; Rush Medical College, Chicago, 1899; associated with St. Joseph's Mercy Hospital in Mason City; died April 13, aged 85.

Herman, Franklin Miller, Rochester, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1896; veteran of World War I; at one time ship's doctor on the Cunard Line from Rio de Janeiro to New York; served on the staff of the Doctors Hospital in New York City; died April 20, aged 88.

Hershberg, David, Los Angeles; Fordham University School of Medicine, New York City, 1917; also a graduate in pharmacy; served on the staff of the Jewish Hospital in Brooklyn; died April 21, aged 71.

Holbrook, George, Keene, N. H.; University of Vermont College of Medicine, Burlington, 1894; died in the Elliot Community Hospital April 14, aged 94.

Holcombe, Virgil Eugene Ⓜ Charleston, W. Va.; born in Lumberton, N. C., Oct. 2, 1894; Medical College of South Carolina, Charleston, 1918; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; in January, 1953, a panel of Logan County citizens selected Dr. and Mrs. Holcombe to be represented in the biographical section of the "History of Logan County," in recognition of their spiritual, educational, and cultural contributions to the county; veteran of World War I; associated with the Charleston General, Mountain State Memorial, and McMillan hospitals; died April 28, aged 64.

Houck, James Sherman Ⓜ Rochester, N. Y.; University of Buffalo School of Medicine, 1921; fellow of the International College of Surgeons and the American College of Surgeons; past-president of the Rochester Academy of Medicine and in 1949 won its merit award; past-president of the Monroe County Medical Society and the Rochester Pathological Society; clinical senior instructor in surgery at the University of Rochester School of Medicine and Dentistry; associated with Genesee Hospital, Park Avenue Hospital, Strong Memorial–Rochester Municipal Hospitals, and the Monroe County Infirmary; died in Los Angeles April 29, aged 62.

Hubbell, Joseph Albert Ⓜ Chicago; Chicago College of Medicine and Surgery, 1917; served in the regular Navy and in France during World War I; died April 29, aged 72.

Huber, William Henry, Glenside, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1898; died April 29, aged 83.

Huvelle, Rene Hector, Litchfield, Conn.; University of Texas School of Medicine, Galveston, 1907; specialist certified by the American Board of Otolaryngology; formerly practiced in New York City, where he was associated with the Manhattan Eye, Ear and Throat Hospital; died April 23, aged 74.

Jones, Wesley Bradley Ⓜ Omaha; Meharry Medical College, Nashville, Tenn., 1918; associated with Doctors and Children's Memorial hospitals; died April 24, aged 67.

Katz, George Heinrich Ⓜ New York City; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1910; associated with Italian Hospital; died March 22, aged 72.

Kemp, Samuel Orestes Ⓜ Albany, N. Y.; Albany Medical College, 1906; associated with the A. N. Brady, St. Peter's, and Albany hospitals; died May 1, aged 76.

Kinney, Earl Ray Ⓜ Ida May, W. Va.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1943; served two years as a captain in the medical corps of the Army, stationed in the Philippines and Japan; physician for the Bethlehem Mines Corporation; associated with Fairmont (W. Va.) General Hospital; died April 29, aged 43.

Kirk, Chalmers Anderson Ⓜ Louisville, Miss.; Memphis (Tenn.) Hospital Medical College, 1903; died in Holly Springs April 29, aged 78.

Klapman, Jacob William Ⓜ Chicago; Northwestern University Medical School, Chicago, 1925; specialist certified by the American Board of *Psychiatry* and Neurology; member of the American Psychiatric Association; formerly on the faculty of his alma mater; veteran of World War I; served as psychiatrist at the Chicago State Hospital; author of "Group Psychotherapy—Theory and Practice"; died in the Alexian Brothers Hospital May 4, aged 60.

Knapp, Howard Clay, Newport Beach, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1928; specialist certified by the American Board of Ophthalmology; certified by the National Board of Medical Examiners; veteran of World Wars I and II and the Korean War; died April 6, aged 57.

Kriegsmann, Adolf Ⓜ Binghamton, N. Y.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1902; died April 5, aged 82.

Leighton, Charles Ⓜ Long Beach, N. Y.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1936; on the staff of the Long Beach Memorial Hospital; died in the Memorial Hospital, New York City, April 26, aged 59.

Lewis, Alfred Lawson Ⓜ Amite, La.; Tulane University School of Medicine, New Orleans, 1916; member of the American Academy of General Practice; served with the American Expeditionary Force in France during World War I; died in the Baptist Hospital, New Orleans, April 25, aged 66.

McCormick, Stuart A. Ⓜ Madison, Wis.; University of Buffalo School of Medicine, 1926; member of the American Psychiatric Association; veteran of World Wars I and II; at one time physician at the state prison at Waupun; for many years physician for the Wisconsin State Board of Control; on the courtesy staff of Methodist Hopsital, where he died April 15, aged 62.

Mabry, William Louis Ⓜ Duncan, Okla. (licensed in Oklahoma under the Act of 1908); veteran of World War I; died March 28, aged 78.

Malloy, Francis V. Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1916; served on the staff of the Veterans Administration; died in the Elgin (Ill.) State Hospital March 15, aged 69.

Medlin, Miles, Marion, La.; Atlanta School of Medicine, 1908; died April 13, aged 81.

Miller, Harry Clay Ⓜ San Diego, Calif.; Detroit College of Medicine and Surgery, 1900; veteran of World War I; for many years practiced in Hillsdale, Mich.; a member of the San Diego Rotary Club; died April 11, aged 84.

Miller, Ralph English Ⓜ Hanover, N. H.; born in Tustin, Mich., Jan. 13, 1899; Harvard Medical School, Boston, 1928; professor of pathology at Dartmouth Medical School, where he served as assistant dean; specialist certified by the American Board of Pathology; certified by the National Board of Medical Examiners; member of the American Association of Pathologists and Bacteriologists, College of American Pathologists, and the American Society of Clinical Pathologists; in 1942 was chosen president of the state board of health; associated with Mary Hitchcock Memorial Hospital; died near Lincoln in February, aged 60.

Neuman, Monroe Eugene, New York City; University of Edinburgh Faculty of Medicine, Scotland, 1931; veteran of World War II; died in the Flower and Fifth Avenue Hospitals Feb. 21, aged 51.

Newell, Edward Ⓜ San Jose, Calif.; College of Physicians and Surgeons, San Francisco, 1905; at one time secretary of the Santa Clara County Medical Society; instrumental in building the San Jose Hospital, where he served on the medical staff; died April 20, aged 85.

Ottenberg, Reuben, New York City; Columbia University College of Physicians and Surgeons, New York City, 1905; specialist certified by the American Board of Internal Medicine; member of the American Society for Clinical Investigation; served on the faculty of his alma mater; served on the staff of the Mount Sinai Hospital; received the Jacobi Medallion for meritorious service to medicine from the Associated Alumni of Mount Sinai Hospital; died in the Mount Sinai Hospital April 25, aged 77.

Peeples, Johnston, Estill, S. C.; Medical College of the State of South Carolina, Charleston, 1911; veteran of World War I; formerly member of the county board of education and for many years served as a surgeon for the Seaboard Airline Railway; on the staff of the Hampton County Hospital; died April 15, aged 71.

Prentice, Arthur Dudley, San Francisco; Cooper Medical College, San Francisco, 1895; retired after 32 years as an epidemiologist with city department of health; veteran of the Spanish-American War; died in the Veterans Administration Hospital April 19, aged 89.

Prince, Arthur, Eastchester, N. Y.; University and Bellevue Hospital Medical College, New York City, 1930; veteran of World War II; served on the staffs of the St. John's Riverside Hospital in Yonkers and the New Rochelle (N. Y.) Hospital; member of the staff of the Mount Vernon (N. Y.) Hospital; died April 12, aged 57.

Reps, Dewey H. Ⓜ Louisville, Ky.; University of Cincinnati College of Medicine, 1925; veteran of World Wars I and II; member of the American Academy of Occupational Medicine and the Industrial Medical Association; assistant medical director of the E. I. Dupont de Nemours & Company's neoprene plant; died in St. Joseph Infirmary April 11, aged 63.

Rieger, Herman Paul Ⓜ Nashville, Tenn.; Baltimore Medical College, 1907; veteran of World War I; on the staff of the Baptist Hospital; died April 16, aged 74.

Ross, Paul Edward Ⓜ Ottawa, Ill.; University of Chicago, The School of Medicine, 1937; member of the American Academy of General Practice; associated with St. Mary's Hospital in La Salle, St. Margaret's Hospital in Spring Valley, and Perry Memorial Hospital in Princeton; on the staff of the Ryburn Memorial Hospital; died in St. Francis Hospital, Peoria, April 13, aged 53.

Ryan, Nicholas Henry, Brooklyn; Fordham University School of Medicine, New York City, 1918; fellow of the American College of Surgeons; past-president of the Kings County Medical Society; taught at the Long Island College of Medicine; on the staff of the Kings County Hospital; secretary of Ryan Ready Mixed Concrete Corporation; died March 27, aged 71.

Schrade, Anna Magdalene Ⓜ Erie, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1902; died March 4, aged 83.

Sharpless, Isaac Ⓜ Rosemont, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1940; veteran of World War II; served as physician of the Philadelphia Ramblers, ice hockey team, Bryn Mawr College, and the Shipley School; member of the executive committee and on the staff of the Bryn Mawr (Pa.) Hospital, where he died April 26, aged 47.

Shelley, Penrose Herr, Port Royal, Pa.; Jefferson Medical College of Philadelphia, 1911; past-president of the Mifflin–Juniata Counties Medical Society; served as school director; veteran of World War I; president of the Port Royal National Bank; on the courtesy staff of Lewistown (Pa.) Hospital; past-president of the Rotary Club; died April 11, aged 73.

Smith, Clifford Addison, Clarington, Ohio; Baltimore Medical College, 1909; died in the City Hospital, Bellaire, April 9, aged 82.

Speer, William Louis Ⓜ Osawatomie, Kan.; Jefferson Medical College of Philadelphia, 1912; member of the American Academy of General Practice; veteran of World War I; in 1945 named Miami county coroner; on the staff of the Miami County Hospital; died April 12, aged 79.

Springer, Ernest Ⓜ Boston; Tufts College Medical School, Boston, 1921; fellow of the International College of Surgeons; member of the American College of Gastroenterology; for many years on the staff of the Massachusetts Memorial Hospitals; on the staff of the Allerton Hospital in Brookline, where he died April 18, aged 60.

Stiles, Francis Augustus Ⓜ Elizabethtown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; died in the Masonic Homes Hospital March 17, aged 83.

Stoelzle, Joseph Daniel Ⓜ Kirkwood, Mo.; St. Louis University School of Medicine, 1920; died Feb. 9, aged 62.

Sullivan, Ralph Charles Ⓜ Oak Park, Ill.; Rush Medical College, Chicago, 1912; fellow of the International College of Surgeons and the American College of Surgeons; on the staff of the Oak Park Hospital, where he died April 29, aged 72.

Swart, William James Ⓜ Schenectady, N. Y.; Albany (N. Y.) Medical College, 1898; formerly a Presbyterian missionary in Siam; for many years physician in the county schools; on the courtesy staff of St. Clare's and Ellis hospitals; died April 6, aged 85.

Swift, Albert George Ⓜ Syracuse, N. Y.; Syracuse University College of Medicine, 1902; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; professor emeritus of surgery at his alma mater; associated with St. Joseph Hospital and University Hospital of the Good Shepherd, where he died April 22, aged 79.

Troupa, Alburt Burton Ⓜ Princeton, Ill.; Chicago College of Medicine and Surgery, 1917; past-president of the Bureau County Medical Society; interned at the Illinois Charitable Eye and Ear Infirmary in Chicago; past-president of the Lions Club; on the staff of the Perry Memorial Hospital, where he died April 1, aged 77.

Willmott, Ashby Carlisle Ⓜ Altadena, Calif.; Kentucky University Medical Department, Louisville, 1901; veteran of World War I; retired in 1947 as surgeon for the Pacific Electric Railway; died in Pasadena April 8, aged 81.

Witt, Dea Cleveland, High Springs, Fla.; University of Tennessee Medical Department, Nashville, Tenn., 1909; served as director of the Bay County health unit; died April 5, aged 74.

FOREIGN LETTERS

DENMARK

Streptococcic and Nonstreptococcic Sore Throat.—Of 81 patients with sore throat this symptom was due to undifferentiated acute respiratory diseases in 36, to streptococci in 34, to mononucleosis in 6, to adenovirus in 4, and to Vincent's infection in 1, as reported by V. Esmann (*Acta med. scandinav.* 163:265-276, 1959). As streptococcic and nonstreptococcic sore throats could not be differentiated on the basis of clinical observations, routine cultures of pharyngeal material for the isolation of beta hemolytic streptococci were made from these patients. An increase in antistreptolysin titer (AST) was found to be a significant sign of streptococcic sore throat, when this increase amounted to 100% of the initial AST, and when the titer in the convalescent phase exceeded 100. An increase in the AST was found to be a significant sign of streptococcic sore throat when the titer in the convalescent phase exceeded 9,000. A significant increase in one or both antibodies was revealed in 50 of the patients. Since the differences between streptococcic and nonstreptococcic sore throat were of a quantitative rather than of a qualitative character, it was difficult if not impossible to decide which of the two types existed in a given patient. Accordingly, a bacteriological study of the pharyngeal flora was important not only in order to secure the diagnosis but also in therapeutic considerations, since penicillin treatment is ineffective against virus infections and therefore contraindicated.

Acute Renal Failure.—A. P. Skouby (*Acta med. scandinav.* 163:277-287, 1959) stated that our knowledge of the underlying mechanisms of acute renal failure was meager and the results of treatment poor. He reported on a series of 56 consecutive patients with acute anuria believed to be due to renal shock. This condition was eventually demonstrated in 37. Limb lead electrocardiograms were found to be of value for differentiating between acute renal failure and uremia due to chronic renal disorders. Apart from conventional methods levarterenol and hydrocortisone were used in pharmacological amounts in selected patients. No secondary actions of levarterenol were detected, and in patients under treatment for one or several days the diuresis increased greatly during the administration.

Hydrocortisone might be of value in the treatment of renal failure in patients with severe primary disorders. No ill-effects were demonstrated. The therapeutic effects obtained depended largely on the basic disorders. In the present series renal shock in most cases appeared as a complication of a severe illness and not as an isolated renal disorder. By treatment of shock and infection the condition of the patients often improved and with the further aid of procedures limiting the influence of renal failure a number of patients recovered. The improvement was often transient, however, and the patients almost always died from the primary disorder, seldom from uremia. Therefore better results might be obtained only by intensified treatment of the basic illness as soon as possible and at least as effectively as with an analogous case in which uremia was not present. Simultaneously, or when the basic illness is under control, procedures curtailing the influence of renal failure might be performed.

Antigravity Suit in Neurosurgery.—P. Freuchen (*Acta anaesth. scandinav.* 3:17-23, 1959) reported that some neurosurgeons preferred to perform certain operations with the patient in a sitting position but that owing to the hydrostatic pressure and the obstruction of the regulation of the circulation this position caused pooling of blood in the lower extremities. To meet these difficulties the author used an antigravity (anti-g) suit which, when inflated with air, exerted a pressure on the patient's legs and lower part of the abdomen. A comparison was made between the effect of the anti-g suit on 14 patients and 14 patients previously operated on for similar disorders in the sitting position with their lower extremities wrapped in elastic or flannel bandages. The use of the anti-g suit made it possible to maintain constant values for pulse rate and blood pressure and thereby maintained optimum conditions for the circulation.

FINLAND

Antibiotics and Immunity.—E. Klemola (*Nord. med.* 61:464-468 [March 19] 1959) commented that in assessing the value of antibiotic treatment a negative factor to be considered was that immunity might be delayed or reduced. It has been shown in animal experiments that early antibiotic treatment in pneumococcic infections and tularemia could reduce immunity. In man recurrences are common in patients with typhoid and paratyphoid treated with chloramphenicol when the treatment is

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The items in these letters are contributed by regular correspondents in the various foreign countries.

stopped too early, as it takes time for immunity to develop. The most important problem concerns the infections caused by beta hemolytic streptococci.

Although penicillin treatment delays and weakens the rise in the antistreptolysin titer (AST), no definite conclusions can be drawn from the AST changes as regards immunity. The fact that despite a good primary effect in scarlatina treated with tetracyclines many bacterial complications caused by the original streptococcic types occur in the weeks after the cessation of treatment could be partly traced to the delayed development of type-specific antibacterial immunity. Scarlatina is a good example of a disease in which antibiotics may delay antitoxic immunity, in this case against an erythrogenic toxin of streptococci. Late second attacks occurring more than three months after the original disease are no longer uncommon. Of 9,400 patients in Stockholm treated with penicillin and with a mean observation period of 2½ years 4.5% had second attacks. Before penicillin was used, and for a period of 10 years, only 1.2% of the patients suffered a second attack.

Of 7,837 patients in Helsinki treated between 1947 and 1956 for a mean observation period of 6½ years, 501 patients or 6.4% had a second attack, of which 1.4% occurred within three months of the first attack and 5% later. The number of cases in which a person acquired scarlatina more than twice is greater than before. In considering the causes of second attacks the moment at which antibiotic treatment is started, the time elapsed after the initial disease, and the degree of severity of the new infection should be taken into account. Although immunity will be reduced if treatment is started early, it is in general desirable to do so because, as stated by the author, the physician concerned cannot take the responsibility for the complications that may arise, all the more as the second attacks are in most cases mild and easy to treat. Except in streptococcic infections the reduction of immunity by antibiotic therapy is probably of no great practical significance. The author concluded that with the discovery of new antibiotics the future situation might be different with regard to both the individual and the community.

GERMANY

Myocarditis and Foot-and-Mouth Disease.—A. Lübke (*Arch. path. Anat.* 332:170, 1959) stated that the hematogenously disseminated foot-and-mouth disease virus penetrates into the myocardial fibrils. The rate and the extent of multiplication of the virus differ from patient to patient and depend on the virus strain. All fibrils are never involved. An abortive increase in the virus may remain optically invisible or may cause only a reversible metabolic disturbance, i. e., fatty change. With a further multiplication of the virus the so-called clumpy degeneration occurs. This usually stops at the intercalated disk. The necrotic fibrils remain rich in virus. Independent of the duration of the infection the virus content of the heart remains high as long as hyalinized muscle fibers or fiber particles are present.

As the necrotic fibers are removed through autolysis and heterolysis the fused particles of virus and fibrillar substance may escape into the circulation. The local neutrophilic reaction is indirectly induced and has little effect on the necrosis. The granulocytes produce no apparent reduction of the virus. In some patients a calcification of the dead fibrils results, but seemingly this does not effect the virus content. The mesenchymal reaction leads finally to a complete replacement of the necrotic fibers (myolysis). During this process the virus disappears from the heart muscle. In the stage of acute inflammatory myocarditis the heart is virus-free, regardless of the duration of the infection. Apparently the macrophages are able to remove not only the destroyed fibrils but also the engulfed virus enzymatically. Seven days after the infection the mesenchymal tissue proliferation begins. The small inflammatory foci ultimately disappear and the large foci heal, leaving scars.

Pulmonary Hypertension.—Esch and Thurn of the University of Bonn (*Fortschr. Geb. Röntgenstrahlen* 90:434, 1959) studied the significance of the following radiologic signs: (1) prominence of the main pulmonary artery segment, (2) widening of the central pulmonary arteries, (3) narrowing of the peripheral pulmonary arteries, and (4) abrupt narrowing at the junction between widened lobar arteries and narrowed segmental arteries. Apart from increased pressure, prominence of the main pulmonary artery segment and dilation of the lobar arteries may be caused by increased blood flow through the lungs. Typical differences in pulsatory behavior were observed. Increased pulmonary blood flow was frequently associated with dilated peripheral arteries. Their behavior under these circumstances was not a reliable radiologic index of the pressure relationships in the lungs. The abrupt change in caliber was the only reliable sign of pulmonary hypertension, even in patients with increased pulmonary blood flow. There was no correlation between the gradual development of the radiologic signs and the height of the pulmonary pressure, although the diagnosis of probable pulmonary hypertension could generally be made on the basis of an ordinary roentgenogram.

Sarcomas.—E. Zeitler (*Strahlentherapie* 108:428, 1959) studied a series of 636 patients with sarcoma and compared the results of purely surgical, radiologic, and combined treatment for the entire series. The five-year survival rate was 30%. The results were better than average in patients with osteosarcoma, fibrosarcoma, and spindle cell sarcoma. The best results were found in those with myosarcoma of the uterus and melanosarcoma of the eye who received purely surgical or combined surgical and radiologic treatment. The three-year survival rate was 50% in these patients. The prognosis was much worse in those with reticulum cell sarcoma, granular cell sarcoma, and lymphosarcoma. The highest three-year survival rate (32.2%), not considering the type of sarcoma, was found in those who received combined surgical and radiologic treatment.

Spleen Cell Suspension for Marrow Damage.—Immediately after whole-body irradiation of inbred rats with 800 rep by high-energy electrons the animals were given an intravenous injection of 100 to 200 x 10,000,000 spleen cells of healthy animals of the same breed, by Thom and Hübner of the University of Heidelberg (*Strahlentherapie* 108:371, 1959). As compared with untreated animals the regeneration of the damaged marrow was more rapid qualitatively and quantitatively. The initial phase of damage was not changed. The first regenerations of the marrow of the treated animals were observed on the third day after irradiation. A complete restitution was observed within 14 days in the treated as compared with 21 days in the untreated animals.

Chronic Leukemia.—The effect of x-ray therapy on survival and duration of illness was studied at the University of Bonn in 132 patients with chronic granulocytic or lymphocytic leukemia by G. Oberhoffer and co-workers (*Strahlentherapie* 108:325, 1959). The duration of illness was not influenced by early or late x-ray therapy. There was no difference in the prognosis in chronic granulocytic or lymphocytic leukemia. The survival time and duration of illness in chronic leukemia were not changed by x-ray therapy, but symptomatic relief was obtained for a short time. Therapy with blood transfusions, antibiotics, cytostatics, and cortisone derivatives also did not change the survival time or duration of chronic leukemia.

Leukocytes and Organisms in Urine.—W. Rupp (*Med. klin.*, vol. 54, 1959) studied the leukocytic and bacterial content of the urine of 690 children (130 boys and 560 girls) with healthy kidneys. The genitals were cleansed with a 0.1% solution of benzalkonium chloride, and 1 or 2 ml. of urine was collected through a sterile catheter. Another sample was then collected in a second sterile test tube, and a bacteriological examination was made within 30 minutes. The leukocyte count was made from the first sample. None of the samples contained albumin. The micro-organisms were counted according to the method of Sanford and the species differentiated by routine bacteriological methods. Between 0 and 10 leukocytes per cubic millimeter were found in samples from 97% of the boys and 93% of the girls, but there was no significant difference between samples from single and repeated catheterization. No micro-organisms were detected in samples from 47.5% of the boys and 37.5% of the girls in single determinations.

In another third of the samples less than 10 micro-organisms were found per milliliter of urine, while more than 10 per milliliter were never found on a single examination. There was no striking difference, on single and repeated catheterization, in the number of micro-organisms detected in the urine of boys or girls. Staphylococcus albus was found in about 50% of all bacteria-containing samples from boys. In 25% of the samples Streptococcus faecalis, followed by Escherichia coli, alpha hemolytic streptococci, Staph. aureus and Proteus vulgaris, was detected. These findings remained essentially unchanged even when a great number of urine samples were examined. In girls the occurrence of only one species of bacteria was not so frequent, and on repeated catheterization beta hemolytic streptococci were more often found than alpha hemolytic strains. Esch. coli and Staph. aureus were definitely found more often in girls than in boys. Staph. albus and alpha hemolytic streptococci were most frequently present in mixed cultures with less than 10 micro-organisms per milliliter, while S. faecalis, Staph. albus, and Esch. coli were more predominant in ranges with more than 10 micro-organisms per milliliter.

These tests confirmed the results obtained by others who had reported a standard number of 0 to 10 leukocytes per milliliter in catheterized and noncatheterized specimens from girls, and this also explained why the slightly enhanced leukocyturia associated with urinary tract infections, especially chronic pyelonephritis, is often not taken seriously and therefore disregarded as a pathological criterion. If the technique is properly employed there should be no irritative leukocyturia even on repeated catheterization. Of the boys examined only once 81% had less than 10 micro-organisms per milliliter of urine, while on repeated examination the percentage rose to 85. The corresponding percentages in girls were 71 and 74.5. In this range Staph. albus was most frequent, followed by alpha hemolytic streptococci and S. faecalis. If there were between 10 and 1,000 organisms per milliliter of urine, Esch. coli was most frequent in girls, whereas Staph. albus was predominant in boys. We may consider 1,000 to 10,000 organisms per milliliter of urine to be the maximum number normally present in catheterized urine specimens from children, and in any case if figures higher than 1,000 per milliliter are reported another specimen should be examined to exclude the possibility of an infection being present.

Lead Poisonings.—J. Lange and co-workers (*Med. klin.*, vol. 54, 1959) reported that as a result of better care and protective measures lead poisoning in the printing trade is no longer common. Lead poisoning now occurs mostly in workmen making dyestuffs and storage batteries. The acute disease is easy to diagnose, but proper treatment is important. Previous attempts to eliminate the lead from the body with potassium iodide, ammonium chloride, calcium salts, dimercaprol, and dihydrotachysterol proved unsatisfactory. These measures aimed at converting the heavy metal into an innocuous depot form. Treatment with edathamel calcium-disodium (EDTA) relieves the abdominal pain of lead poisoning within a few days without producing side-effects. EDTA was given to five persons who had a history of lead poisonings. In two of these lead was excreted from the urine, although they had not been in contact with lead for three years. Controls trials were carried out on six healthy volunteers, and even in these a slightly increased urinary excretion of lead was observed, which indicated that lead intake may occur in persons with no professional contact with this element. Although the drug used binds and thus eliminates not only lead but also magnesium, copper, and iron, this did not result in any undue depletion of the body's essential stocks of these substances. It was further shown that lead anemias in patients treated with EDTA improved without additional iron therapy.

Mastocytosis.—D. Remy of Hamburg, at the meeting of the German Society of Internal Medicine at Wiesbaden in April, stated that urticaria pigmentosa can no longer be considered an isolated skin disease. Although it is characterized by cutaneous symptoms, it affects other organs. It consists in mast cell infiltrations of the subcutis and mast cell proliferation in the reticuloendothelial system, especially the spleen, liver, and bone marrow. In some patients the cutaneous symptoms predominated but in others they were absent, although an accumulation of mast cells in the reticuloendothelial system could be demonstrated. The increased release of histamine caused urticaria in some patients and in others severe circulatory collapse with an extreme drop in blood pressure, usually preceded by an erythematous flush. Vomiting and fever might occur at the same time. In these patients remissions alternated with severe circulatory crises.

Further symptoms are characterized by hyperheparinemia, which leads to an increased tendency to bleeding, shifts of the lipoproteins of blood serum with a marked lowering of cholesterol and phospholipids, and deviations of the lipid electrophoretic pattern. Elevated excretion of decomposition products of serotonin was not observed in the author's series although this has been described by others. Other signs included skeletal changes (especially osteosclerosis), gastric hyperacidity and occasionally ulcers partly due to hyperhistaminemia, and motor and secretory disturbances of the small intestine. The disease bears a nosological relationship to mast cell leukemias, although the peripheral basophil count is usually not increased in the latter. It appears justified, however, to speak of a mast cell leukosis. A close relationship to plasmocytoma and the lymphoreticuloses seems to exist, and mixed forms have been occasionally observed.

Nicotinic Acid Amide Metabolism.—At the same meeting N. Gerlich reported that he had treated a series of 504 patients who had internal tumors with bis-ethylenimino-benzoquinone and tris-ethylenimino-benzoquinone. The limitations of such cytostatic treatment were set not only by the toxic leukopenia and thrombocytopenia that developed with adequate doses but by also general symptoms appearing and growing progressively worse with prolonged therapy (atrophy of nails and of gastrointestinal mucosa, dryness and scaliness of the skin, and depression). The leukocyte count remained at about 3,000 per cubic millimeter. The clinical symptoms corresponded to those of hypovitaminosis.

An increasing deprivation of nicotinic acid amide developed during prolonged treatment. Recent findings by Holzer and co-workers suggested that the ethylenimino compounds lowered the diphosphopyridine nucleotide (DPN) concentration. These cytostatic products are capable of alkylating nicotinic acid amide as pyridine nitrogen. Nicotinic acid amide and also nicotinic acid can therefore compensate the effect of ethylenimino-quinones. The experimental hypovitaminosis produced by prolonged cytostatic treatment causes death when not counteracted. The reduction of DPN concentration exerts no effects either in the tumor itself or throughout the body.

INDIA

Serum Proteins in Gestoses.—M. K. K. Menon and co-workers (*Journal of Obstetrics and Gynecology of India,* vol. 9, March, 1959) estimated the serum protein levels in patients with preeclampsia and eclampsia and in the babies born to these mothers. Estimations were also made to determine whether there were any variations in these values after delivery and the establishment of lactation. Patients with preeclampsia only 34 to 40 weeks pregnant and showing edema, albuminuria, and hypertension were included in the study. They were further divided into those with grade A (mild) and grade B (severe) conditions. Only antepartum eclamptic patients were included. The first sample of blood was collected in the acute phase of the disease, and further samples were taken 48 to 96 hours after delivery. There were 47 patients with preeclampsia grade A, 9 with grade B, and 42 with eclampsia.

Estimations of serum protein levels were made in 17 babies of mothers with grade A and in 7 of mothers with grade B preeclampsia, and in 17 of mothers with eclampsia.

There was a significant drop in the total serum protein levels in all the toxemic patients as compared to the values in normal pregnant patients. The fall in the albumin fraction was not statistically significant in patients with grade B preeclampsia and in eclampsia but it was markedly significant in those with grade A preeclampsia. Even more significant was the reduction in the globulin fraction, the beta and gamma globulins showing a greater fall than alpha-1 and alpha-2 fractions. Thus the fall in total serum proteins was due to a fall in both the albumin and globulin fractions, the reduction being more significant in the latter. The variations in the values of serum proteins in patients with grade B preeclampsia and eclampsia were almost identical but were statistically different from those observed in patients with grade A preeclampsia. The total serum protein level and its fractions showed a higher value in grade B preeclamptic and eclamptic patients as compared to grade A preeclamptic patients, probably due to hemoconcentration which was believed to exist in these patients.

The values were, however, lower than those obtained in normal pregnant patients. The variations in serum protein levels observed 48 and 96 hours after delivery were similar to those after normal pregnancy. Thus the albumin showed a fall after delivery but slowly increased at 96 hours. The mean value of globulin slowly increased soon after the birth of the child and more after 96 hours. The total protein level showed a small drop at 48 hours, but by 96 hours the values had reached and passed the preparturient level. The serum protein levels in babies born to toxemic mothers reflected the same variations from normal as were observed in the mothers themselves. Thus the total protein levels and albumin and globulin fractions were reduced in babies born to mothers with preeclampsia and eclampsia, the fall in the beta and gamma globulin values being statistically significant.

Dysfunctional Uterine Bleeding.—Shah and Dave (*Journal of Obstetrics and Gynecology of India*, vol. 9, March, 1959) defined dysfunctional uterine bleeding as abnormal bleeding in the absence of a neoplastic, inflammatory, or chorionic lesion. It includes conditions of the endometrium resulting from disturbed endocrine function and others in which no abnormality is revealed by ordinary histological examination. A series of 35 patients with this condition between the ages of 13 and 39 years were studied, and of these 5 were later found to have an organic lesion of the uterus. The endometrium was studied in 27 of the remaining 30 patients. No single endometrial pattern was associated with dysfunctional uterine bleeding, although in most patients the changes in the endometrium conformed to those of the proliferative phase or of hyperplasia cystica glandulosa. Thus in this study 15 patients showed proliferative changes, 7 showed hyperplasia, and 5 showed typical secretory phase. In most of the patients a single endometrial biopsy specimen and vaginal smear were obtained prior to treatment. A differential count was made from 200 to 300 normal squamous epithelial cells of each vaginal smear and the percentage of cornified and basal or parabasal cells determined. If there was a cervical erosion, or an infection of the cervix or vagina existed, the determinations from these patients were dropped from the study.

Androgen therapy was started if the vaginal cytological findings were suggestive of high estrogen activity. The dosage was 25 mg. of the hormone daily for three days and later every second or third day. Smears were repeated after administration of 100, 150, 200, and 250 mg. and at the end of treatment. Endometrial biopsy specimens were also taken if possible. The total dosage usually ranged between 150 and 250 mg., spread over two to four weeks. Once bleeding stopped ethinyl estradiol orally and progestrone parenterally were given in a cyclic fashion for 5 to 12 consecutive cycles. Androgen therapy was advocated in patients who had 40% or more of cornified cells in their vaginal smears. This was indicated in 16 of the 30 patients. When properly guided by vaginal smear examination, this therapy was found to give beneficial results in most such patients.

After about 100 mg. of testosterone was given the effects of estrogen neutralization were observed by reduction in the number of cornified cells and a proportionate increase in precornified or intermediate cells. With further administration there was greater reduction in the cornified cells and the appearance of basal cells. The dosage of androgen required in different patients for physiological neutralization of estrogen was variable. In the dosage employed in this study it not only helped in stopping the bleeding but also probably helped in normalizing the basic dysfunction in some patients with anovulatory bleeding. Although vaginal cytological study helps in deciding the hormonal therapy, microscopic examination of the endometrium cannot be omitted entirely as organic lesions of the uterine mucosa might thus be missed. Tuberculosis of the endometrium was responsible for 3 of the 35 cases in this study which would have remained undiagnosed if no endometrial biopsy had been performed.

Cholera.—According to a report issued by the World Health Organization 1958 was a bad year for cholera. The number of cases which occurred in Asia (about 93,000) was the highest recorded since 1953, when the disease struck 242,000 people.

Epidemics occurred last year in India, Pakistan, Thailand, and Nepal. The worst epidemic was in the lower Ganges valley in eastern Pakistan, where 20% of all cholera cases for the year were reported. Several districts in India were also severely hit, and there were 4,895 cases with 1,765 deaths in Calcutta alone.

Malignant Hypertension.—Pinto and Shah (*Journal of the Association of Physicians of India,* vol. 7, March, 1959) studied a series of 22 patients with grade 4 hypertensive encephalopathy. The onset was acute in 6 patients and gradual in 16, some of them learning that they had hypertension only after they came to hospital. Most of the patients were between 20 and 40 years of age and none was over 50. The systolic pressures varied between 270 and 180 mm. Hg and the diastolic pressures between 194 and 94 mm. Hg. Six patients received no hypotensive drugs, 13 were treated with ganglion blocking agents, and 3 were given hypotensive agents. None was treated by Kempner's rice diet alone, but one who did not respond to large doses of pentolinium compound showed a significant fall in blood pressure after being put on this diet for 14 days and then given small parenteral doses of pentolinium.

The results indicated that a combination of pentolinium compounds administered subcutaneously and Rauwolfia derivatives given orally, preceded by two weeks of the rice diet, was the most effective treatment, while oral administration of mecamylamine and Rauwolfia derivatives was the most convenient form of treatment. The use of ganglion blocking agents helped to prolong the life of patients with malignant hypertension. Thus, while only 1 of the 6 untreated patients survived, 5 of the 13 treated with ganglion blocking agents were discharged with a marked reduction in both systolic and diastolic blood pressures and complete relief from distressing symptoms.

The progress of two patients was followed for two years, and they were still normotensive when last seen. Of the patients treated with ganglion blocking agents seven showed marked subjective and objective improvement, three showed a moderate improvement, and in three there was no improvement. Complete relief of symptoms was obtained in those in whom the blood pressure showed a marked fall. The symptoms were not relieved in those who responded with moderate or poor fall in blood pressure. The retinopathy improved in 3 of the 22 patients with improvement in vision.

In the same issue M. J. Shah and co-workers reported a series of 14 patients with hypertensive encephalopathy, the incidence of which appears to be declining although that of hypertension is increasing. Therapy with intravenously given sucrose was used as a dehydrating measure with no adverse effects in five patients, and 50% dextrose solution was given to 7. Magnesium sulfate solution was given to 11 patients per rectum. Lumbar puncture was performed on only one. Ganglion blocking agents were given to five and Rauwolfia alkaloids to four. Of the 14 patients 5 were treated with dehydrating measures alone, and of these 4 died; 9 received antihypertensive drugs in addition to dehydrating measures, and of these only one died. One patient showed a precipitous and uncontrollable fall of blood pressure, after a parenteral dose of pentolinium tartrate, which proved fatal; one patient who was given hexamethonium developed a residual permanent hemiplegia.

Blood Sugar Levels and Glycosuria.—Sathe and Ajgaonkar (*Journal of the Association of Physicians of India,* vol. 7, March, 1959) tried to correlate blood sugar levels with renal threshold and the degree of glycosuria and assess the value of these findings in the interpretation of the status of diabetes, in a series of 34 diabetics whose ages varied between 25 and 75 years. The 24-hour urinary volume gave no indication of the severity of diabetes; 24-hour urinary sugar excretion levels, although useful in assessing the progress of the disease, were not a reliable guide because the renal threshold varied during treatment. Estimation of the sugar level in fasting urine samples was also misleading. Urine passed two hours after a full meal was the only fairly reliable guide, provided the renal threshold was not too high. The severity of diabetes could not be assessed from the fasting blood sugar levels. The authors concluded that a glucose tolerance test should be made whenever possible to assess the diabetic state and elicit the renal threshold.

Diethylcarbamazine and Tropical Eosinophilia.—S. S. Misra and co-workers (*Journal of the Indian Medical Association,* vol. 32, March 16, 1959) treated 40 patients who had tropical eosinophilia with diethylcarbamazine. The absolute eosinophil counts were over 4,000 per cubic millimeter in these patients; stool and sputum specimens were negative for any parasitic infection; the night blood film was negative for Microfilaria bancrofti on three consecutive occasions; and radiologically most of them showed the findings of eosinophilic lung disease. Dry cough, dyspnea, and wheezing were present in all. Sternal marrow smears were made from all patients. The total and differential leukocyte counts were repeated after four days of oral therapy with the drug. Subsequently leukocyte counts were made as frequently as necessary until they came down to normal. An absolute eosinophil count and sternal marrow smear were repeated at this stage. For oral therapy most adults received 12 tablets of 50 mg. each per day in 3 or 4 divided doses, while children were given 8 or 9 tablets in divided doses. Of the eight patients treated parenterally the first four patients were given 800 mg. of the drug intramuscularly and the rest were given three or four injections of 400 mg. each at intervals of three to five days.

Of the 32 patients receiving oral therapy 31 were cured. By the fourth day there was either complete or partial relief. Symptomatic relief was almost always prompt. These 31 patients had a complete remission of physical signs at the end of therapy. The eosinophil counts showed a definite fall within four days in 16 patients and in the rest the count came down gradually. The time taken for complete remission of eosinophilia varied widely. Sternal puncture was done before starting and after termination of therapy in 14 patients. In all it showed hyperplasia and predominance of immature and mature eosinophils at the start of the therapy, while sternal smears after therapy showed only a few eosinophils, most of which were mature. The maximum duration of therapy was 30 days. Most patients required treatment for 10 to 16 days. There was an almost complete lack of toxicity, most of the patients tolerating the drug well. Some had anorexia and nausea. There was no correlation between the duration of illness and the length of required therapy.

Two patients who had earlier proved resistant to arsenic were given this drug with gratifying results. The quick symptomatic relief without the initial symptomatic aggravation often produced by arsenic, absence of relapse, ease of administration, and shorter duration of therapy as compared with arsenical treatment were some of the advantages. The intramuscular therapy with this drug, however, proved disappointing. Nausea, vomiting and drowsiness occurred in all patients. Some had giddiness, dryness of the mouth, and itching all over the body. One developed such marked respiratory depression that he had to be kept in an iron lung for several days. The symptoms and signs were aggravated, and there was an increase in the eosinophil count. Of the four patients receiving 800 mg. by injection only one was cured, while toxic reactions were seen in all. In those who received three or four injections of 400 mg. there was only symptomatic relief with a decrease in blood count, but the blood picture did not return to normal. Six of the eight patients who received parenteral therapy later responded to oral doses of the drug, and one was cured with arsenic.

Medical Teaching.—In his presidential address to the Association of Physicians of India Dr. Bhatia made a strong plea for raising the salaries of the teaching staffs of medical colleges. He said that medical colleges should have some full-time teachers, but the faculties should be supplemented by paid part-time and honorary teachers. He saw no reason why the top medical teachers should not be paid the same emoluments as are given to judges, civil service secretaries, or professors of engineering. The union government has issued a circular to the state governments directing them to maintain nonpracticing teaching posts on very low salaries. If the government's directive is carried out, further deterioration in the standards of medical education will occur. It is essential that some of the teaching be given by teachers conversant with treatment in the home environment—the type of treatment most of the graduates will have to give when they start their practice. The speaker suggested that university examinations be gradually dispensed with and students be given credit for day-to-day work.

Experimental Tuberculosis.—M. Sirsi (*Journal of the Indian Medical Association*, vol. 32, March 16, 1959) stated that the strain of the organism, the host species, and the physiological state of the host at the time of vaccination influenced the development of immunity. Thus certain physiological and nutritional disturbances have been shown to favor multiplication of BCG and cause progressive lesions leading to the death of the animal. Nutrition plays a prominent but varying role in the development of susceptibility or resistance to infection in various diseases, influencing both multiplication of the organism and antibody production. Nutritional deficiencies are common in school children who are given BCG vaccination in the mass campaign. The development of hypersensitivity to tuberculin is taken as an index of the resistance to tuberculosis conferred by BCG. The tuberculin reaction can be modified by various environmental factors, including vitamin deficiency.

The author studied the results of deficient nutrition on the immunological response to BCG vaccination by challenging immunized animals with virulent tubercle bacilli and noting the effect on the course of the disease. Albino mice known to be susceptible to tuberculosis were used. After a preconditioning period, when the animals were kept on a diet supplying only 30% of their nutritional requirements, they were immunized with 0.1 mg. of BCG vaccine given intraperitoneally. One month was allowed for the development of immunity, after which a virulent human strain of Mycobacterium tuberculosis was injected intravenously. For comparison various control groups of animals, immunized and nonimmunized and on both adequate and insufficient diets, were studied simultaneously. The degree of development of resistance to tuberculosis was assessed from the survival period and weight loss noticed in these animals. It was concluded that vaccination with BCG alone had no adverse effect on the growth of the mice in both the well-fed and underfed groups, while the degree of protection offered by BCG vaccination in the underfed group was in no way inferior to that seen in well-fed group.

Experimental Hydrocephalus.—Nigam and Singhai (*Indian Journal of Surgery,* vol. 21, February, 1959) injected intrathecally (1) 40 and 50% suspensions of India ink, (2) a 20% suspension of kaolin, and (3) a 12-weeks' culture of a bovine strain of Mycobacterium tuberculosis to produce hydrocephalus in dogs and white rats. Some animals died immediately after the injection. The brain, meninges, and proximal part of the spinal cord in those that died or were killed were studied for gross and microscopic changes. The Prussian blue test was used in some to demonstrate the site of obstruction to the flow of spinal fluid. India ink was used in 24 adult rats and 5 dogs; 14 rats and 3 dogs received single injections and the rest had repeated injections up to a maximum of three, the interval between injections being three to six weeks.

Three of the rats died immediately. Ten rats and five dogs showed signs of meningeal irritation, looking ill and lethargic and showing apathy toward food two to three weeks after injection. All the rats had fever, head retraction, deviation of the eyeballs, and loss of weight. One dog developed quadriplegia and another signs of cranial enlargement. The dye was found distributed in the subarachnoid space mainly in the meninges, the maximum deposition being in the basal cisternae and along the vessels in the sulci of the cerebral and cerebellar hemispheres. The duras were devoid of ink except at the site of injection. The pia-arachnoids were studded with ink. The dilated ventricles of the rats, in contrast to those of the dogs, contained ink. The meninges were thickened and adherent at the site of injections in half of the specimens from rats and all from dogs. The brain proper was completely devoid of ink. Half of the rats showed dilatation of the cerebral ventricles. Three of the four dogs showed symmetrical dilatation of the ventricles. In both the anterior horns of the lateral ventricles were most affected. The third and fourth ventricles and cerebral aqueduct were also dilated. The intraventricular foramens were widely patent. One specimen showed only unilateral dilatation of the lateral ventricle. The cerebral cortex was atrophic. Microscopically India ink was seen in the lining cells of the arachnoid with leukocytic infiltration and with perivascular deposition of ink along the Virchow-Robin spaces. Hydrocephalic specimens showed atrophy of periventricular structures, especially the basal ganglions and corpus callosum, with edema of the nerve cells. There was ependymal flattening but the choroid plexus was not involved.

M. tuberculosis was injected into 18 rats, half without prior sensitization and half first sensitized by a subcutaneous injection of the dead bacilli followed by intrathecal injection of living bacilli three weeks later. There were no immediate deaths. All had repeated injections at intervals of four to eight weeks, up to a maximum of three. Only two of the unsensitized and one of the sensitized animals showed definite hydrocephalus. About 40% showed evidence of meningeal irritation, which was not so marked as with India ink. No bacilli were detected in the smears prepared from exudates at the site of injection. Kaolin suspension was injected into 13 rats. Seven died immediately. Of the six surviving animals two showed meningeal irritation and hydrocephalic changes. Others showed no pathological change. Of the three agents used India ink was thus most suitable, the immediate mortality being only 13% and meningeal irritation and dilatation of ventricles being seen in 50%.

The dogs showed a higher incidence of hydrocephalus than the rats with the same agent. The most frequent site of dilatation was the anterior horn. Dilatation was not related to the time elapsing after the first injection or the number of injections. The hydrocephalus was found to be of a communicating variety as evidenced by the Prussian blue test. Two specimens showed arachnoid cysts, probably a result of chronic meningeal irritation.

Protein Content of Breast Milk.—Mukherji and Anwikar (*Indian Journal of Paediatrics,* vol. 26, January, 1959) stated that malnutrition is the greatest single problem in the care of children. Of 12,935 children seen during a period of 11 months in an outpatient clinic 1,589 or 13.6% suffered from gross nutritional deficiency. Of the latter 7% showed evidence of protein deficiency, either in the form of nutritional edema or frank kwashiorkor. Of all the hospital admissions in the same period 5% showed nutritional edema or kwashiorkor. More than 33% of the children attending the hospitals for some other complaints suffered from varying degrees of deficiency of essential food factors. Many cases of nutritional edema were found in children who were breast fed for a prolonged period. Although most cases of kwashiorkor occurred when the child was being weaned, some were seen in children who were still breast fed, mostly after 9 to 12 months. This may have been because the quantity of the milk received by the baby was insufficient or because the protein content of the breast milk of these mothers was significantly lower than normal.

The mothers studied came from poor and malnourished families. Their protein intake was low during both pregnancy and lactation, all of them having had no milk and little animal protein in their diets. They were all overworked and anemic and had had a large number of pregnancies at short intervals. Miscarriages and/or early death of the child occurring soon after birth and due to malnutrition or infection was frequent. Twenty such mothers whose children were admitted with nutritional edema or kwashiorkor and who were still nursing their babies had their breast milk analyzed for protein. Thirty-six lactating mothers served as controls. The duration of lactation in the protein-deficient group was nine months to three years and in the control group it was two months to five years. The results were classified according to the age of the child and age, diet, and parity of the mother.

The micro-Kjeldahl method was used to estimate the total nitrogen content of the sample of breast milk, and the protein content was calculated from this figure. The plasma protein levels were estimated in 10 of these children. In the control group the mean level of protein in the breast milk was 1.34 Gm.% while in the 20 mothers whose children showed signs of protein deficiency the mean protein content of the breast milk was 1.13 Gm.%. Both the upper and lower limits of the protein content of breast milk of control group were slightly higher than those of the group under study. The difference was, however, not marked, the malnourished group showing only a slight diminution in protein content. There was no relation between the parity or age of the mother and the protein content of the breast milk. The plasma protein levels in the children were uniformly low, ranging between 2.8 and 5.3 Gm.%.

Syphilitic Survey.—Nagesh and Kutty (*Indian Journal of Dermatology and Venereology*, vol. 25, Jan.-March, 1959) analyzed the results of 2,000 Venereal Disease Research Laboratory (VDRL) and Kahn tests. Serums that showed strong positive reactions to both tests were regarded as truly positive, while those showing a positive reaction to the VDRL and a negative reaction to the Kahn test were regarded as false-positive, requiring further observation. Often they indicated an early stage of syphilis. Of the 2,000 specimens 310 reactions turned out to be truly positive and 232 were false-positives. Twenty-five of the specimens were spinal fluid and the results with these were uniformly negative. A specimen showing a negative VDRL reaction to the test was not subjected to a Kahn test, since the former is the more sensitive test. Although the VDRL test is sensitive it is not highly specific for syphilis, and a positive result of the VDRL test was taken as a pointer to be confirmed later for the probable existence of syphilitic infection. It is, however, a good test for screening out all definitely negative syphilitic serums.

Hydrocortisone and Osteoarthritis.—Tiwari and Bhargava (*Indian Journal of Surgery*, vol. 21, February, 1959) treated 80 patients who had osteoarthritis with intra-articular injections of hydrocortisone. In most patients the usual methods such as massage, radiant heat, compound mercurial ointment, and therapy with salicylates had been tried with no significant relief. Of 16 patients with knee involvement who received deep x-ray therapy 13 obtained relief. The position of the needle inside the joint was confirmed before injection by aspirating a drop of synovial fluid. After injection the joint was moved through its full range and a firm bandage applied for 24 hours. The amount of hydrocortisone used for each joint was determined arbitrarily. The amount used for single injection was 50.0 mg. for the hip, 25.0 mg. for the knee and shoulder, 12.5 mg. for the wrist and ankle, and 5.0 mg. for interphalangeal joints. The injections were repeated after the return of symptoms or after 48 hours, if no relief followed the first injection.

As a rule relief was experienced 24 hours after injection, pain and a slight effusion developing in the first few hours. No relief was expected if it did not appear within 48 hours. The period of relief varied from one week to more than a year and was three to six weeks in most patients. Early recurrence was observed if the limbs were abused or used excessively. An optimum quantity of the drug was required to produce relief in each joint, but an increase beyond this amount did not influence the duration or amount of the relief. There was no relationship between the severity of the radiologic findings and the extent of relief produced by injection.

After 3 months 32 patients, after 6 months 18, and after 12 months 3 showed no radiologic improvement, while in 2 the condition was aggravated although the joint was free of symptoms. In most, however, the process seemed to have been arrested as shown by repeated roentgenograms. Of the 13 patients with involvement of the knee joint who responded to deep x-ray therapy 12 obtained good results with intra-articular hydrocortisone and one fair results. Of the three who did not respond to deep x-ray therapy one obtained a good result with hydrocortisone and two failed to respond. Thus the results obtained with these two types of treatment are probably similar. Complications included increase in pain 8 to 10 hours after the injection in 52 patients accompanied by warmth and local tenderness in 34 and slight effusion in 9. In patients who responded to the therapy this pain subsided within 24 hours. There was no relationship between the severity of this pain and the possible success of the treatment. Successive injections usually caused less pain. Sepsis did not occur in any of the patients and there were no side-effects of the drug. The results were gratifying in most of the patients treated.

ISRAEL

Tuberculosis.—S. Btesh of the Ministry of Health (*Israel M. J.* 17:241, 1958) stated that mass immigration to Israel after 1948 was associated with an increased incidence of tuberculosis. This disease was not prevalent in the settled Palestinian Jewish population during the period of the British Mandate (1918-1948). This was in part due to the high ratio of young people among the settlers, the relatively high standard of living and housing, and the satisfactory level of medical care. The tuberculosis death rate which in 1948 was 18 dropped to 5.1 per 100,000 population in 1957. Between July, 1948, and the end of 1951 687,000 immigrants entered Israel under a policy of free and unselected immigration. The Yemenite and Iraqi Jewish communities were transported to Israel in toto. Nearly half of these new arrivals were examined. In 288,000 persons examined over 4,000 patients with active tuberculosis were found to have entered Israel during this period. The new arrivals had a prevalence ratio of about 0.6%, as against 0.1% for the settled population in 1947, but the prevalence of tuberculosis among immigrants showed a steady decline from its peak of 0.92% in 1948 to 0.25% in 1951. The highest incidence (0.93%) was found in the immigrants from Turkey and the lowest (0.08%) in the Yemenites.

More significant, perhaps, than the difference in prevalence ratios was the type of tuberculous lesion found. Among 2,090 patients of European origin 0.6% had primary infections, 22% minimal lesions, 68% moderately advanced lesions, and 9.4% advanced lesions. Among 1,648 patients of Asian and African origin, the respective percentages were 5.8, 28.2, 56, and 10. In addition to these differences in prevalence and type the further course of the disease was modified by a number of important factors. These included the degree of resistance of each group to the disease, the unsatisfactory food supply in the country from 1948 to 1953, poor housing and sanitary facilities, the mass case-finding and BCG inoculation campaigns after November, 1948, the routine hospitalization of patients with active infection, and the introduction of modern chemotherapy and surgical treatment.

Due to mass immigration the incidence of tuberculosis among the Jewish population rose rapidly from 5.1 per 10,000 in 1947 to 21.3 per 10,000 in 1950. Many of the immigrants from eastern Europe had been in concentration camps, and about 40,000 arriving in 1948 had also been interned on Cyprus after attempts at "illegal" entry into Palestine. This group exhibited a high morbidity and mortality from tuberculosis in the years after immigration and showed a high incidence of tuberculin reactors. Although most of the pre-1948 Jewish settlers also came from eastern Europe they were a selected group who had immigrated under more favorable conditions between the two world wars. Their morbidity and mortality from tuberculosis were lower than those of the later immigrants from the same countries, and lower than the average for the whole Jewish population. The incidence among them of positive tuberculin reactors was also much lower than among the immigrants. European Jews are known to have a high tuberculosis infection rate, with relatively high resistance and low death rates. The adverse environmental factors of the war years in Europe produced an increased death rate from tuberculosis in this group. The high morbidity and mortality found among eastern European Jewish immigrants were due to the initial high infectivity plus a lower resistance resulting from the stresses of World War II and the period immediately preceding their immigration to Israel.

Immigrants from Yemen coming in 1949 and 1950 had low prevalence rates (0.08%) but in the following years they proved to be extremely susceptible to tuberculosis, and their morbidity and mortality rose rapidly. In 1952 the morbidity was 19 per 10,000, and the mortality 44.4 per 100,000, but by 1957 these figures had dropped to 14.6 and 19.1. The established Yemenite population of Israel comprised about 16,500 Jews, who had immigrated in small groups between 1918 and 1948. Their tuberculosis morbidity after 1952 was similar to that of the newer immigrants, with neither the infection rate nor the susceptibility differing significantly in the two groups.

The Jewish communities of North Africa are scattered over Libya, Tunisia, Algeria, and Morocco. The North African immigration between 1948 and 1950 consisted of about 100,000 unselected persons coming mainly from Tunisia and Morocco. The prevalence of active tuberculosis among this group was not high (0.23%). In 1954 the prevalence of tuberculosis in the Jewish ghettos of Morocco and Tunisia was about 0.17% and it was much lower among the Jews from the Atlas Mountains region. The low infection rate among this group is further indicated by the relatively low incidence of the disease in the first few years after immigration, although it rose steadily to a peak in 1954 (13.2 per 10,000 morbidity, 13.5 per 100,000 mortality). The Asian group included 120,000 immigrants from Iraq, 30,000 from Iran, and a few from Syria, Lebanon, Afghanistan, and Kurdistan. The prevalence of tuberculosis was similar in all groups, about 0.2%, as was the progress of the disease in this population after immigration.

On the whole, the Jewish communities of the Arab countries and Iran (Yemen excepted) did not live in isolation nor were they segregated in ghettos. Many immigrated to Israel in 1950 and 1951, the Iraqi community being transplanted in toto while the immigration from Iran was free and voluntary. Prior to 1948 there was a large established community in Palestine originating from the Arab countries and Iran. The morbidity and mortality studies of this settled group showed no significant difference from those of the new immigrants from the same countries. Both groups had a fairly high resistance to tuberculosis: 0.2% morbidity and 5 per 100,000 mortality, in 1957. In 1935 the prevalence of tuberculosis among Palestinian Jews was 0.39% and 0.38% for urban and rural Jews respectively. Corresponding figures for the Arab population were 0.66% and 0.53%. The most striking finding was the high morbidity rate of the Bedouin nomadic tribes living in the southern desert of Israel. Their contact with other segments of the population had always been minimal, but in the past few years these tribes have tended to restrict their wanderings and have increased their trade relations with the settled population. Their low resistance to tuberculosis is shown by the high morbidity and by the acute form which the disease frequently takes. The morbidity in Bedouins was 0.27% in 1955.

JAPAN

Breast Cancer.—At the 15th quadrennial Medical Congress in Tokyo in April it was reported that the incidence of death from breast cancer in Japan is less than 16% of that in United States. The rate is increasing, however. Dr. Hirayama made a study which led him to conclude that (1) the incidence of breast cancer was highest in women in the menopause and in the upper economic level, (2) with mothers who were pregnant only once or twice the incidence of breast cancer was about three times as great as in those who had had a greater number of pregnancies; (3) the incidence in those who married after reaching the age of 25 years was twice that of those who married earlier, (4) the incidence in those who had had mastitis was twice that in those who had not, and (5) the incidence in women who smoked was significantly higher than that in nonsmokers and in those who ate meat than that in vegetarians. Among the victims of breast cancer the incidence was far greater in those who stopped breast feeding early. In the rural areas the mothers nurse their babies for a year or longer while in the city they switch to bottle feeding much earlier. Among unmarried women, for whom the question of breast feeding does not arise, the incidence of breast cancer is low compared to that of unmarried women in the United States.

Thermal Anesthesia.—At the same meeting Drs. Muto and Watanabe described a new type of anesthesia. Whereas heretofore the low limit of temperature for thermal anesthesia had been considered to be 30 C (86 F), the authors reduced the body temperature of dogs to 10 C (50 F) for three hours, and to 15 C (58 F) for two hours. The circulation entirely ceased, giving an effect similar to that achieved by the mechanical heart. In human subjects the temperature was lowered to 25 C (77 F) with use of ice packs and cold air. This method of anesthesia was used in a series of 168 patients ranging in age from 2 days to 76 years. To hasten recovery massage, electric shock, and stimulants were used. The other advantages of thermal anesthesia were the simplicity and safety of technique, minimal loss of blood, and rapid recovery.

NORWAY

Paranoid Incidents, Delirium, and Amphetamine.—F. Askevold (*Acta psychiat. et neurol. scandinav.* 34:145-164, 1959) reported a series of 14 patients who were admitted to Ullevaal Hospital because of amphetamine addiction. Of these patients seven either were hospitalized with an acute paranoid psychosis or had undergone one or more such psychotic episodes prior to admission. These episodes were transitory and disappeared in a few days. None of the patients suffered from a prolonged schizoid attack. In the other seven, all of whom had abused other drugs, no psychotic symptoms were apparent; but they showed sleeplessness, irritability, or suspicion related directly to the use of amphetamine. The reactions might be interpreted as a continuum in which the individual disposition, the amount of amphetamine taken, and the admixture of other substances were the factors deciding the nature of the reaction. The psychotic reactions were regarded as toxic psychoses, and it was suggested that they were connected with the effect of amphetamine on the mechanism of cerebral oxidation. Four patients developed delirium during the withdrawal of the drug. In these patients a common symptom complex was evident, different from that seen in the delirium associated with alcoholism, morphinism, and barbiturism. The characteristic difference was the lack of anxiety and the only slight vegetative symptoms, while activity and restlessness were greatly increased. There was also a lengthy latent period and the delirium lasted longer.

SWEDEN

Cytological Testing for Cancer of the Uterus.—Early in 1956 Dr. A. Pelzer organized a cytological laboratory at the gynecologic hospital of Malmö. By the end of September, 1957, he had personally examined cell smears from 2,000 women about whom he reported in *Svenska läkartidningen,* March 26. Many of them had uterine bleeding but some had no symptoms. The smears were usually taken from both the fornix and the os uteri and were stained according to the Papanicolaou method. In 1,623 cases two smears were examined. The smears were classified as positive, doubtful, or negative in terms of malignancy. Attached to the positive reports was an attempt to define the histological type of cancer cell identified. No such tentative diagnosis was ventured when cells were scarce or staining was imperfect. Whenever the verdict was "positive" or "doubtful" an exploratory excision or curettage was undertaken, no treatment being given without such preliminary tests. Among the 69 women found to have cancer of the uterus the cytological test was reported as negative in only 5. In 12 the tests resulted in an early diagnosis of malignancy. The author hopes that with improved technique in taking and treating smears, as well as with more experience in their interpretation, these findings can be improved on.

Hospital Beds for Mental Disease.—The latest report (*Svenska läkartidningen*, April 17, 1959) of the Government commission appointed in 1955 to investigate the care of the mentally ill is concerned only with adults, and it shows how time and again the authorities have failed to supply the necessary number of beds. At the turn of the century it was calculated that 3.4 per 1,000 of the population required hospital beds for mental disease. This meant about 10,000 beds; but the 12 mental hospitals then available had only about 7,000 beds in all. In 1945 when 25,000 beds were needed only 18,000 were available. An official report in 1950 sounded a more hopeful note for, although about 3,000 more beds were needed than were available, it was hoped that the gap between need and supply could largely be closed by speeding up the turnover. In 1954, however, the gap between the two was about 5,000 beds. The problem of closing this gap is complicated by the upward shift in elderly persons in the community and by changes in the relative numbers of certain mental diseases, with schizophrenia and manic-depressive psychosis less frequent and reactive psychoses, alcoholism, and the psychopathies more frequent. The psychoses of old age have also become relatively more frequent. Meanwhile about 40% of the appointments of medical officers in Sweden's mental hospitals are vacant for want of applicants.

Lung Cancer and Smoking in Twins.—The dogma that smoking causes lung cancer has been challenged on the ground that persons of a certain temperament may be more likely to smoke tobacco than persons of a different temperament, irrespective of extraneous factors. A hereditary factor, hitherto inadequately explored, and the development of lung cancer in persons who happen to smoke has been postulated. Following this line of thought Prof. L. Friberg and co-workers in Stockholm made a study of twins. They believe that a common factor may predispose to disease as well as to excessive smoking. If, they argue, it is found that identical twins are more alike in smoking habits than nonidentical twins, then constitutional factors may significantly influence these habits. A series of 59 monozygotic and 59 dizygotic pairs of twins were interviewed or sent a carefully worded questionnaire. The degree of concordance of smoking habits within the monozygotic and the dizygotic pairs was investigated (*British Medical Journal*, April 25, 1959) and shown to be significantly greater within the monozygotic pairs.

UNITED KINGDOM

Ulcerative Colitis and Cancer of the Colon.—Rosenqvist and co-workers (*Lancet* 1:906, 1959) studied a series of 500 patients with ulcerative colitis and concluded that one such patient in three develops carcinoma if the disease is present for 10 to 20 years. Since carcinoma of the colon is highly malignant and often difficult to diagnose, colectomy is indicated as a prophylactic measure. Much has been written about the psychosomatic origin of ulcerative colitis and the use of psychotherapy in its treatment. Rosenqvist pointed out that by the time these patients are hospitalized the condition may already be precancerous or even malignant and that psychotherapy and the removal of possible stress factors are no longer important. Relative freedom from the symptoms of ulcerative colitis does not insure that cancer will not develop. On the contrary 26 of the patients were completely or almost free of symptoms for several years before the lesions became malignant. One of the patients had been free of symptoms for 12 years.

Minister Accused of Delay.—Mr. Walker-Smith, Minister of Health, was severely criticized by the House of Commons Select Committee on Estimates for delaying an inquiry into the possible misuse of the domiciliary consultation service, a delay that is contrary to the public interest. The service provides for a specialist to go to the home of a patient when requested by a family physician. The issue arose in the autumn of 1957 after expert evidence that the number of house calls seemed inordinately high. It was claimed that family doctors frequently failed to attend with the consultant. There had been a rise in the number of house calls made by full-time specialists since they became entitled to payment in 1955. The report called attention to the fact that it was originally stated that Mr. Walker-Smith was taking steps to institute inquiries, but that he had gotten no further than to consider the form of an inquiry.

Mr. Walker-Smith stated that, since the need for a domiciliary consultation is essentially a question of clinical judgment in individual circumstances at a particular time, it is difficult to devise methods of ascertaining whether misuse of the service exists. The committee recommended that if the previous evidence was not contradicted by information now sought, the inquiry should be made without further delay.

Hospital Equipment Exhibition.—A reconstruction of the laboratory at St. Mary's Hospital where Sir Alexander Fleming discovered penicillin was shown at the second International Hospital Equipment and Medical Services Exhibition in London, in May.

Most of the material for this exhibit was collected by Lady Fleming, who continues to work in the laboratory. It is intended for a permanent museum which will later be housed in the Wright-Fleming Institute at St. Mary's. The exhibit included an authentic reproduction of the dish in which Sir Alexander first observed the lifesaving mold, Sir Alexander's microscope, and many manuscripts and awards never before seen by the public. Alongside the reconstructed laboratory there were examples of the latest equipment for producing penicillin.

The development of surgery and its debt to science and engineering was illustrated by examples of modern surgical equipment and of instruments used in hospitals of the 17th and 18th centuries. Old prints of hospital scenes from the 16th to 18th centuries were lent by hospitals and museums. A section devoted to electromedical equipment showed how defects in or damage to the blood stream, brain, and heart can be accurately diagnosed before operation. A model of a 2,000,000-volt machine used in the treatment of cancer and now in use in several British hospitals was flown from Canada. An iron lung and apparatus which can replace vital organs, such as the lungs and heart, during operations were also shown.

District Nurses.—Few towns and villages are without a district nurse. Patients who need treatment at home, including a large proportion of the old and the bedridden, are completely dependent on her. The service of which she is a member celebrates its centenary this year. It will therefore surprise many people to find that the Queen's Institute of District Nursing is finding it necessary to launch an appeal for $700,000. The reason is that district nursing has not been wholly integrated into the National Health Service (NHS). Its running costs are charged to the state, but the training of nurses is not. Local health authorities contribute to a certain extent, but most of the expenses of training must still be found by voluntary contribution. More than 700 nurses are trained every year and the costs have risen steeply. The question arises whether the district nurses should be taken over entirely by the NHS. Some believe it is a salutary thing that the welfare state should still leave room for voluntary contributions and private charity.

Radiation Hazards in Hospital.—A committee was appointed by the government in 1956 to study the dangers of the diagnostic and therapeutic uses of radiology, inspired by a Medical Research Council report on the hazards to man of nuclear and allied radiations. The committee, consisting of one or more physiologists, radiologists, gynecologists, and authorities on the medical use of radioactive isotopes, has made its report (Radiological Hazards to Patients, Her Majesty's Stationery Office, 1959). It considers that mass radiography, if properly conducted, is safe, and that the benefits far outweigh the slight risk. Nearly 5,000,000 persons have chest films taken by mass radiography each year. These examinations bring to light 18,000 cases of tuberculosis and 63,000 other abnormal conditions of the chest annually, including 2,362 cases of cancer of the lung and 12,000 cases of heart disease. Thus every year 80,000 cases of crippling or fatal disease are discovered in the early stages before the patient has symptoms. According to the committee the indefinite continuation of mass radiography at its present rate would not add more than 20 cases of leukemia to the annual incidence of 2,500 cases and might produce none at all. In any case this is a small price to pay for the benefits received. The committee stressed the possibility that patients might refuse the benefit of diagnostic and therapeutic radiology because of widespread misleading publicity on the hazards of irradiation.

The committee laid down certain safeguards. The dose of radiation should be the minimum consistent with the taking of a good film. Scatter and extraneous radiation should be reduced as far as possible, and mass radiography should not be used in children or pregnant women. In making its report the committee surveyed the numbers and types of radiographic examinations being made, the number of films used, and the apparatus available in hospitals and clinics. Measurements were made of the dose of radiation received by patients undergoing different types of radiographic examination.

New Radioactive Hazard.—New radioactive hazards to industrial workers are the "go-devils" used by oil, gas, water, and other industries for detecting whether newly laid mains are free from obstruction and for the routine maintenance of existing pipelines. Go-devils are tightly fitted rubber washers, scraper vanes, or wire brushes mounted on a central core. They are pushed through pipelines by means of water or compressed air, and they sometimes get jammed against an obstruction. Determination of their exact location can be time-consuming and costly, involving excavations over a long length of pipeline if this runs underground. The inclusion of a radioactive tracer in the central core, which is exposed on contact with an obstruction, overcomes the difficulty of detecting the position of the go-devil. Then it can be detected above ground by a Geiger counter. The handling of this radioactive material has become another industrial hazard, and a code of practice was recently laid down to prevent unnecessary exposure of personnel.

Physicians and the Press.—At the Royal Society of Health congress in Harrogate the anonymity of the medical profession was criticized in a discussion of the relationship between doctors and the press. Dr. W. S. Parker said that one of the most difficult problems to be overcome was the reticence of physicians in discussing professional matters and in making any comment on topics of medical interest. More contact should be made between the medical profession and the public through the press, which at present is a neglected route. While the reticence of individuals should be maintained, contact with the public could be made intelligently and in language that could be understood. He advocated a grant from the National Health Service budget toward health education. As little as 1%, invested in such a program, would pay handsome dividends. These views were supported by Dr. Harvey Flack who urged that physicians who are governed by outmoded ethical rules cast aside their inhibitions and give journalists positive, forthright statements that could be quoted. There is a need for doctors who can express themselves accurately and responsibly to the ordinary layman. The editor of the *News Chronicle* said that it was the doctors' duty to keep the public informed. They tended to devalue their role in keeping the community healthy. The medical profession and the press must come to terms on the best methods of informing the public about preventive medicine. Even with poliomyelitis the public had not been given a clear impression of the facts or it would have cooperated better in the vaccination campaign.

The medical correspondent of the *Observer* said that before the press could educate society it must enlist the help of the medical profession. Some physicians laid the blame on the press. Dr. J. Burn attacked the press for unhealthy publicity on legalized abortion, artificial insemination, and other matters, but he believed the press could play a great part in health education. Other speakers blamed the press for distorting statements made to them by doctors. Some of the delegates stated that it was not the function of the press to educate its readers. In their opinion health education was better done through the schools and colleges and directly by the physician.

Poisoning from Marking Ink.—An outbreak of methemoglobinemic cyanosis in six newborn babies due to the absorption of aniline dye from their diapers was reported by Ramsay and Harvey (*Lancet* 1:910, 1959). The first case occurred in an infant who became cyanotic on the 8th day of life and passed numerous loose green stools. Routine blood studies showed no abnormality but in view of the extreme cyanosis the blood was examined spectroscopically and intense absorption bands of methemoglobin were observed. Ascorbic acid (200 mg.) and methylene blue (5 mg.) were injected intravenously and within 15 minutes the infant's skin became a normal pink color. The cause of the cyanosis was not suspected until five other babies in the same hospital were found to be similarly infected. Inquiry revealed that new diapers were normally marked with colored cotton thread but owing to a defect in the sewing machine they were marked on this occasion with an indelible ink made from an aniline dye. All the affected babies were given new diapers marked with this dye. Aniline dyes in marking ink are known to be absorbed percutaneously and to cause methemoglobinemia. Once the cause was recognized and the source of poisoning removed the babies recovered without any specific treatment.

Obstetric "Oil, Bath, and Enema."—The administration of castor oil, followed by a soap enema and a hot bath, is one of the oldest and most frequently attempted methods of inducing labor. Because of its unpleasant features many obstetricians have abandoned the use of castor oil. Mathie and Dawson have assessed, with the aid of a tocograph, the possible effects of this procedure on uterine contractility in late pregnancy (*Brit. M. J.* 1:1162, 1959). Sixty women who were between 38 and 41 weeks pregnant were divided into four groups, excluding those who appeared likely to have an abnormal labor and those showing any sign of the onset of labor. The first group had a complete OBE (castor oil, hot bath and enema); only castor oil was given to those in the second; only the enema to those in the third; and only a hot bath to those in the fourth group. The changes in uterine activity in each patient were assessed by the guard-ring tocodynamometer. This instrument is claimed to provide an absolute measurement of the changes in intra-amniotic pressure and thus of uterine contractions. The head of the instrument was applied to the anterior abdominal wall over a fluid-filled part of the uterus and held in place with a stiff elastic belt passed around the abdomen. From a study of the tocographic tracings the amplitude in grams per square centimeter and the duration and frequency of each contraction were calculated.

The tracings showed that a complete OBE produces a marked increase of uterine activity, increasing the contractile work done by the uterus by an average of 264%. The administration of castor oil alone increased the contractile work by an average of 186%, and a soap enema alone increased it by 95%. A hot bath alone had no significant effect. In the control group studied there was a spontaneous variation of uterine activity in the course of three hours with a mean of –4%. The authors therefore concluded that the marked increase in uterine activity produced by an OBE justifies its retention in obstetrics. Only the castor oil and enema played a significant part, but the hot bath had other advantages.

CORRESPONDENCE

MUSCLE WORK AND BODY TEMPERATURE

To the Editor:—A few years ago an article, by Karpovich, on the subject of warming-up exercises appeared in The Journal (Nov. 17, 1956, pp. 1117-1119). The author recently referred to it in an international publication. The subject is of immense interest to athletes throughout the world and to all those engaged in research in this sphere. Since Karpovich's writings, as well as reports in the *Research Quarterly*, indicate that certain facts connected with the problem may not be generally known, knowledge of procedures in previous research is of value in further study in this field.

About 50 years ago Prof. J. Lindhard, founder of the Copenhagen University Gymnastic Theoretical Laboratory, found that an athlete had a rectal temperature of 40.5 C (104.9 F) immediately after completing a run (*Gymnastikteori* 2:135, 3:288, 1918). Since the "normal" body temperature is 37 C (98.6 F), what was the cause of this unexpected high temperature?

This subject was investigated by Dr. Marius Nielsen (*Skandinav. Arch. f. Physiol.* 79:193-230, 1938), whose study was made on men who worked in the nude. As these men worked, their body temperatures (inside the trunk) and skin temperatures were measured by thermoelectric means. The work, measured on a Krogh stationary cycle ergometer, with rates varying from 360 to 1,440 kg.-m. per minute (in one case for a duration of 4½ hours), was carried out at the Copenhagen University Zo-ophysiological Laboratory. The room temperature was varied from 5 to 36 C, which affects the body's heat regulation by convection and radiation; the humidity of the air was increased from 50 to 80%, affecting the heat regulation by evaporation; and there were fans to move the air, affecting the heat regulation by convection.

It was found that the body temperature rises to a definite and constant level, the height of which is determined by the intensity of work. The body temperature, within a wide range, was unaffected by the room temperature, unaffected by the humidity of the air, and also unaffected by moving the air by fans. The rise of the body temperature was practically proportional to the oxygen intake. At rest the body temperature was about 37.0 C (98.6 F); at work rates of 360, 720, 1,080, and 1,260 kg.-m. per minute, the body temperature rose to 37.4 C (99.3 F), 37.8 C (100.0 F), 38.2 C (100.8 F), and 39.0 C (102.2 F), respectively.

Therefore, when we say that the normal body temperature is 37 C, we must add "when the body is at rest." It is just as normal to have a body temperature of 39 C during a work rate of 1,260 kg.-m. per minute for some time. Another fact is that it takes 30 to 50 minutes to raise the body temperature, depending on the work rate. From these facts we may conclude that the center for the regulation of the body temperature is not failing to function accurately during intensive muscle work; on the contrary, the body temperature seems to maintain its level more exactly during muscle work than at rest.

Another question arises: What is the organic "reason" for high temperature during muscle work? Pavlov once said that nervous centers act and react in a most intelligent way in relation to stimuli from the surroundings. It is worthy to note that athletes know from experience that it is unpleasant to perform, and especially to compete, in an event if they feel cold, and so they instinctively jump and swing their arms or do other vigorous exercises before the athletic event. Ballet dancers also work vigorously before going on stage.

Dr. Marius Nielsen points out that chemical processes accelerate in higher temperature. It is also known to athletes and ballet dancers that it is more pleasant to perform when the body is warm than when it is cold. This brings us to the articles by Karpovich (*FIEP*, bull. 2, 1958; *Springfield Coll. Bull.* [Feb.] 1957) in which he fails to find advantages in preliminary warming-up exercises.

Asmussen and Bøje's study (Asmussen: *Tidsskr. f. Legensøv.* no. 3, 1939; Asmussen and Bøje: *ibid.*, no. 2, 1945; *Acta Physiol. Scandinav.* 10:1, 1945) indicates that high body temperature as a result of warming-up exercises is advantageous and that the more vigorous the warming-up exercises the better the athletic results (of certain types). This, of course, demands that the athlete be in a good condition and able to stand prolonged and vigorous warming-up exercises as well as the following event, and he must do his warming-up exercises and perform in the event without any pause for rest.

It might seem strange that Hale and Karpovich fail to find warming-up effective while Asmussen and Bøje found distinct improvement as a result of warming-up exercises. The reason for such conflicting results probably is to be found in their different methods of study. The fact that a runner broke a record without warming-up, as Karpovich points out, can hardly be accepted as convincing proof. Records were broken in years past when the problem of warming-up was unknown. Furthermore, records are broken not during training but at sports meetings and presumably partly as a result of the stimulating effect of the excitement, i. e., the additional concentration of epinephrine.

When Asmussen and Bøje, at Copenhagen University, studied the effect of warming-up on physical performance, consisting of a sprint of 35 pedal revolutions on a Krogh stationary cycle ergometer, which in physical output is more or less equal to a running sprint of 100 m., they used the following procedure. All experiments for a period of about five weeks were made in the mornings. The subjects were between 21 and 39 years of age. Some of them were well-trained sportsmen, some were nonsportsmen, and others were professional cyclists. Some were of the leptosome type, and others were of the athletic and pyknic types. Arriving at the laboratory in the mornings, the subjects had a 30-minute resting period of lying down before the experiment began, whether they did warming-up exercises or not. Warming-up exercises consisted of 30 minutes of cycling on a Krogh stationary cycle ergometer and were done at a work rate of about 600 kg.-m. per minute. On alternating days the sprint (35 pedal revolutions) was performed without preliminary warming-up, immediately after the 30-minute resting period.

They found that the times for the sprint in all subjects were better with preliminary warming-up exercises. A typical graph shows that a subject's average time was 13.7 seconds without warming-up but 12.6 seconds with preliminary warming-up, which is an improvement of 1.1 seconds (or 8%).

Asmussen and Bøje made a similar study but on 450 pedal revolutions, which in physical output is about equal to a 1,500-meter run. Here again was found a noticeable effect of preliminary warming-up exercises. A typical graph from this study shows that a subject had an average time of 4 minutes and 39.7 seconds without preliminary warming-up but 4 minutes and 25.2 seconds with preliminary warming-up, which is an improvement of 13.5 seconds (or 5%). There should be no resting period between the warming-up period and the following event. More recent studies show that the effect of warming-up diminishes by an intermediate period of rest, i. e., the longer the period of rest the less effective is the preliminary warming-up. Best results are achieved after a warming-up period of 30 to 50 minutes, but 10 to 15 minutes of warming-up exercises also result in some improvement in the following event. Warming-up exercises should preferably be performed with the muscles which are to be used in the event. The athlete's training condition must be such that he can endure vigorous and prolonged warming-up exercises as well as the event without an intermediate period of rest. Warming-up exercises may not be beneficial to athletes in preparation for activities of very long duration, such as marathon running.

The above reports may be of interest to athletes and, perhaps, to investigators who might use them as bases for further research.

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DISCUSSIONS AT BEDSIDE

To the Editor:—As one of a small group of Fellows of the American College of Physicians, I had the privilege last April of attending lectures at El Instituto Nacional de Cardiologia, in Mexico City, and meeting its renowned director, Dr. Ignacio Chavez. I was impressed by this unique, modern center of cardiology, not only by the buildings and the newer devices for detection and treatment of heart ailments but also by the down-to-earth awareness that all this was for the treatment of ordinary human beings who were in distress. Dr. Chavez, whose scientific achievements are equaled by his charm as a host and his dedication to his patients, was justifiably proud when he showed us through this great institution. One of his greatest satisfactions came from a room at the end of each ward in which were only a table, a few chairs, and some reference books. He said:

> This is our talking room. Let me make myself clear by telling you a . . . story. Once, while making rounds in the children's section, I overheard two youngsters . . . not more than six years old. One said: "I've got a rheumatic heart murmur in my mitral valve." The other, not to be outdone, answered: "Oh, that's not so much. I've got a double aortic murmur. It's more serious than yours." It was then that . . . it became hospital policy never to discuss a patient at his bedside. If tots could become "little doctors" just by listening to our bedside discussions, think how much iatrogenic disease we spread when in earshot of grownups. Now we take necessary notes at the bedside, and after rounds we all . . . [go] to our talking room where we can discuss treatment and prognosis without fear of adding unnecessary burdens of anxiety to an already sick patient.

While many American institutions have adopted a similar policy, from personal observation I know that there are still too many doctors who "think out loud," not only at their patient's bedside but also during office management. The art of medicine has lagged behind its sister, science. We must keep reminding ourselves that we treat human beings, not case histories. That's all there is to the art of medicine.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Augmentation: A Third Stage of Digitalis Therapy. E. H. Blackard and T. R. Harrison. A. M. A. Arch. Int. Med. 103:543-550 (April) 1959 [Chicago].

The authors studied the effects of administering gitalin, a short-acting digitalis preparation, to the point of minor toxic manifestations in 33 patients with congestive heart failure. Of these, 18 had been treated by other physicians according to the accepted method of initial digitalization followed by administration of the standard maintenance dosage with various preparations. All 18 were supposedly optimally digitalized and were referred to the authors because of refractory heart failure. It was found that these patients were actually underdigitalized, and most of them were able to take within a few days one-half to 2 of the usual full digitalization doses before minor toxic symptoms developed. All of them showed subjective improvement, and 11 showed undoubted objective evidence of improved cardiac function. In 7 of the 11 the improvement was apparently due to digitalis alone.

These observations indicated that the current standard methods of administering digitalis are inadequate and that periodic augmentation is desirable in patients who are having symptoms despite receiving the drug in the usual accepted maintenance dose. For such augmentation a short-acting digitalis is to be preferred because of the brief duration of such minor toxic effects as anorexia, nausea, and weakness. For the most desirable results of improved cardiac function, precautions should be observed during periods of augmentation as follows: 1. The patient should take the drug himself and only after meals and provided the appetite shows no sudden decrease. 2. During the period of increased dosage the patient should be seen at least once daily by a physician. 3. Potassium chloride should be administered with each dose of digitalis during the supplementary period. 4. A clear distinction should be made between anorexia and nausea due to digitalis and symptoms resulting either from abdominal congestion (which is usually an indication for more digitalis) or from concurrent disease, such as uremia, or from such drugs as ammonium chloride, morphine, or aminophylline. 5. It should be recalled that premature beats are frequently due to the underlying cardiac disorder as such, and that under such circumstances they may be abolished by digitalis. Rarely, this is true for bigeminal rhythm.

Of the 33 patients to whom gitalin was given to the point of minimal untoward effects, 25 (75%) showed gastrointestinal symptoms without evidence of cardiotoxicity. In only 3 was the reverse observed. No serious toxic effects were seen. It is suggested that periodic augmentation of the dosage of digitalis should be employed, with the previously listed safeguards, in patients who are failing to show satisfactory control of congestive heart failure.

Asian Influenza A in Boston, 1957-1958: I. Observations in Thirty-Two Influenza-Associated Fatal Cases. C. M. Martin, C. M. Kunin, L. S. Gottlieb and others. A. M. A. Arch. Int. Med. 103:515-531 (April) 1959 [Chicago].

The authors report on 14 female and 18 male patients, between the ages of 11 and 71 years, with Asian influenza A who died in the Boston area between August, 1957, and March, 1958. The clinical courses, laboratory findings, and autopsy findings in these patients were similar to those associated with fatal cases during earlier influenza epidemics. Of the 32 patients, 12 had advanced heart disease, and 10 had either chronic intrinsic pulmonary disease or chronic respiratory insufficiency secondary to neurological or neoplastic disease. Four women died during pregnancy. Fifteen patients had influenza without bacterial complication, 11 had postinfluenzal staphylococcic pneumonia, and 6 had postinfluenzal nonstaphylococcic bacterial pneumonia. Influenzal and postinfluenzal pneumonias thus were the commonest and severest complications. Bacterial, and particularly staphylococcic, pneumonia, when it occurs in adults after influenza, is generally severer and more rapidly progressive than it is under other circumstances. The frequent occurrence of hemoptysis, tachypnea, and cyanosis in the patients suggests that these symptoms, with or without prominent pulmonary findings, are highly indicative of potentially fatal disease. The interval between the time when severe disease was first recognized and the time when death occurred was 48 hours or less in 25 patients (81%). In a consider-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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able proportion of the patients with severe influenza, the bacteriological, roentgenographic, and other laboratory techniques used were not effective in distinguishing between pure influenza and postinfluenzal bacterial pneumonia rapidly enough to be useful for specific treatment.

Strains of Asian influenza A virus were isolated from antemortem throat washings or postmortem tissues in 14 (44%) of the 32 patients, and, by means of fluorescein-labeled antibody techniques, influenza A viral antigen was shown in interstitial macrophages of respiratory tract tissues in 9 patients (31%). Except when Gram-stain studies of sputum revealed specific pathogens or when roentgenographic studies revealed pulmonary cavitation, it was not possible to make a prompt diagnostic differentiation between pure influenzal pneumonia and postinfluenzal bacterial pneumonia. It is suggested that in times of epidemic influenza, and in areas in which staphylococcic infections are highly prevalent, patients presenting with the signs usually associated with fatal influenza should be treated promptly as having bacterial pneumonias, unless or until that diagnosis is disproved. The need for a practical "artificial lung" to support patients in the acute respiratory insufficiency of severe influenza is emphasized.

Asian Influenza A in Boston, 1957-1958: II. Severe Staphylococcal Pneumonia Complicating Influenza. C. M. Martin, C. M. Kunin, L. S. Gottlieb and M. Finland. A. M. A. Arch. Int. Med. 103:532-542 (April) 1959 [Chicago].

The authors compared the findings, clinical course, and management in 11 patients with Asian influenza A who had fatal postinfluenzal staphylococcic pneumonia, and were reported on in the preceding paper, with those in 9 patients with nonfatal staphylococcic pneumonia following Asian influenza A, who were observed and studied in Boston and environs during the pandemic of that disease in 1957-1958. The fatal cases were generally marked by severer and more rapidly progressing illness, less accurate diagnosis, and relatively ineffective antibiotic therapy. Although most of the 20 cases of staphylococcic pneumonia arose in the community rather than in hospitals, the strains of staphylococci responsible for the occurrence of pneumonia were commonly resistant to multiple antibiotics and were of bacteriophage types most often associated with hospital-acquired infections.

Disk sensitivity tests performed directly on sputum or body fluids containing staphylococci afforded a rapid, relatively accurate guide for the selection of effective antibiotics. Although the antibiotic combination of erythromycin and chloramphenicol, with or without novobiocin, was most often associated with survival of the patients, the number of patients was too small and the treatment schedules too varied to state with certainty the superiority of any one effective regimen over another. It is suggested that during epidemic influenza, in areas in which major staphylococcic infections are common, all patients with the signs of potentially fatal influenza be diagnosed and treated promptly as having staphylococcic pneumonia caused by the prevalent types of antibiotic-resistant staphylococci until the diagnosis can be disproved.

Serum Aldolase in Muscle Disease. R. A. Thompson and P. J. Vignos Jr. A. M. A. Arch. Int. Med. 103:551-564 (April) 1959 [Chicago].

The authors determined the serum aldolase level in a series of patients, children and adults, with neuromuscular diseases manifested primarily by skeletal muscle weakness. The serum concentration of aldolase was elevated in patients with primary myopathy including degenerative and inflammatory muscle disease, such as polymyositis, muscular dystrophy, and dystrophia myotonica. The highest serum aldolase levels were determined in patients with polymyositis and in patients, between the ages of 3 and 15 years, with muscular dystrophy. The level of serum aldolase in patients with muscular dystrophy decreased with increasing age, diminished muscle mass, and reduced functional ability. Serum enyzme levels appear to have prognostic value in patients with muscular dystrophy, since there is a positive correlation between net loss of muscle mass and serum enzyme concentration.

Patients with muscle weakness due to neurogenic atrophy or impairment of conduction at the neuromuscular junction had a normal serum aldolase level. This finding is a helpful differential diagnostic aid in separating these patients from those with primary myopathies. Determinations of serum aldolase level may give valuable assistance in regulating steroid therapy in patients with polymyositis. Biochemical changes in muscle as reflected by a decrease in aldolase serum levels precede clinically demonstrable improvement in muscle strength.

An Assessment of Long-Term Anticoagulant Administration After Cardiac Infarction: Report of the Working Party on Anticoagulant Therapy in Coronary Thrombosis to the Medical Research Council. G. Pickering, W. M. Arnott, R. Biggs and others. Brit. M. J. 1:803-810 (March 28) 1959 [London].

There has been little agreement on the efficacy of anticoagulant therapy in lowering the risk of death or recurrent infarction. The main aim of the clinical trial here reported was to establish whether, in patients who had survived at least one month after their most recent infarction, the continuous administration of an anticoagulant drug (phenindione), in doses sufficient to double the one-stage "prothrombin" time, would appreciably reduce the risk of recurrence and death below the levels concurrently observed in a series of patients with illnesses of comparable severity, given tablets containing only 1 mg. of phenindione. The 383 patients who had recovered from the acute phase of a cardiac infarction of defined severity were classified according to their previous infarct history and allocated at random within each hospital center to these high-dosage and low-dosage series. Both groups of patients were seen at regular intervals every 2 or 3 weeks and were clinically assessed more fully by roentgenologic and electrocardiographic methods every 3 months. Laboratory control was maintained by Quick's test of the one-stage "prothrombin" time, and in the high-dosage series the amount of the drug administered was adjusted to ensure a level 2 or 2½ times the control value. Three indexes of the effectiveness of the regimens were used: (1) death from all causes, from cardiovascular disease in general, and from recurrent myocardial infarction in particular; (2) frequency of myocardial reinfarction of varying degrees of severity; and (3) subsidiary data on return to work and the presence of anginal pain or dyspnea at the time of the last examination. A note was made of all incidents, such as embolism and hemorrhage, which might be affected by the anticoagulant therapy.

Comparisons were made between the outcome in different subgroups of patients and at different stages of the follow-up period which ranged up to a maximum of 3 years. The analysis was as follows: 1. Although the death rate was higher in the low-dosage series, there is just the possibility that the difference could have occurred by chance. No difference was apparent in women, but the numbers were too small to exclude such a difference. 2. When infarcts serious enough to cause permanent withdrawal from the trial were added to deaths as a combined index of prophylactic failure, there was a significant reduction in their frequency among men receiving the high doses; and there was a suggestion of a better result in men under the age of 55 years. 3. The same trends appeared even more clearly when the total reinfarction rate was used as the basis of comparison. Under the age of 55, men on high doses suffered recurrent infarctions at only one-fifth the rate of those on low dosage, and over that age the rate was halved by high dosage. These differences are statistically significant. 4. The proportionate reduction in the risk of reinfarction achieved by the high-dosage regimen was slightly greater among patients with a previous history of one or more infarcts, but the difference is not statistically significant. 5. The difference in the death rate was most evident in the first 6 months of the follow-up period, but the disparity in the reinfarction rate was maintained for at least 2 years of the follow-up period. 6. More men given the higher doses returned to work during the period, and they were more often free from angina. 7. There were 15 withdrawals from the high-dosage series because of the onset of conditions actively or potentially associated with hemorrhage.

Four major cerebrovascular accidents—3 causing withdrawal and 1 death—were reported in the high-dosage series. Only 1 patient on low dosage suffered a cerebral hemorrhage, but embolism was a major complicating feature in the terminal illness of 3 patients. There were 48 minor hemorrhagic incidents in the high-dosage group compared with 8 among those on low dosage. The authors compared these results with those in 2 similar studies and found close agreement in many respects with one of these clinical trials. It appears that phenindione administered continuously in the conditions of this trial can make a useful, if limited, contribution in the after-care of patients who have recovered from the acute phase of myocardial infarction.

Subacute Pulmonary Hypertension Due to Chorionepithelioma. **K. D. Bagshawe and W. D. W. Brooks. Lancet 1:653-658 (March 28) 1959 [London].**

The term "subacute pulmonary hypertension" has been applied to the condition produced by carcinomatous metastases in the lungs. Three forms have been described: (1) carcinomatous lymphangitis in which the lymphatics are extensively invaded by cancer cells causing compression of alveoli and capillaries without invasion of the blood vessels; (2) carcinomatous lymphangitis in which cancer cells from the perivascular lymphatics compress and invade the small arteries and arterioles producing a pulmonary endarteritis which may be followed by intravascular thrombosis; and (3) a pure embolic form in which the pulmonary arteries and arterioles are occluded by cancer-cell emboli and secondary thrombosis.

The purely embolic form seems to be rare. One of the few reported cases of this form was mentioned by McMichael in 1948 in a review of pulmonary heart disease, and the authors describe this case here together with 2 others. The patient reported in 1948 and one of the 2 other patients died. These 2 women presented with dyspnea, cyanosis, pulmonary hypertension, and low cardiac output. They were found at autopsy to have chorionepithelioma confined to the pelvic veins and pulmonary arteries. The third patient has similar clinical features and a high gonadotropin titer and is thought to have a similar pathological process, though neither diagnostic curettage nor careful histological examination of the uterus showed the presence of chorionepithelioma.

The diagnosis is difficult. Only 1 of the 3 cases presented was diagnosed while the patient was still alive, but after considerable delay. In one of the fatal cases thyrotoxicosis was suspected, and pulmonary embolism was suspected as the cause of the chest pain. In the second case a right-to-left intracardiac shunt was considered. While distinction from simple emphysema is not difficult, tuberculosis has been mimicked in some cases. Differentiation from subacute thromboembolism will be difficult, since the basic mechanisms in the 2 conditions are similar. Distinction in the absence of a pelvic tumor will be possible only by means of biological tests for gonadotropic activity. It therefore seems desirable to perform such a test in all cases of thromboembolism in women of menstrual age.

The presentation with subacute pulmonary hypertension of 2 patients with latent chorionepithelioma within a period of 14 months under the care of one physician suggests that the condition may be less rare than the literature indicates. Such cases may have been diagnosed as thromboembolism or as idiopathic pulmonary hypertension. Interest in chorionepithelioma, which is usually rapidly progressive, has been heightened by reports of new methods of treatment. Prolongation of life has probably resulted from the use of nitrogen mustard. Because chorionic tumors are fetal in origin and therefore of different genetic structure from the maternal tissues, it has been suggested to transfer tissue from the husband to the patient with the object of increasing her antigenic response to the tumor cells. The one surviving patient of the 3 presented here showed a good response to treatment with anti-folic-acid and antipurine drugs in high intermittent dosage. This treatment had been suggested by Hertz and others in 1958 and had effected remissions in a number of patients.

Botulism in Arctic Alaska: Report of 13 Cases with 5 Fatalities. E. S. Rabeau. Alaska Med. 1:6-9 (March) 1959 [Anchorage].

Five outbreaks of botulism in Arctic Alaska are reported. At Kotzebue in 1947, 3 persons developed clinically typical botulism, and 2 died; and in 1948 there were 2 cases, with one fatality. In 1950 at Point Hope, 5 cases of nonfatal botulism occurred, and the organism, Clostridium botulinum, type E, was isolated in some of the remaining food. In 1952, near Selawick, one case occurred with death. At Kotzebue in 1956, 2 cases, with one fatality, occurred. In both the last 2 outbreaks, Cl. botulinum, type E, was identified. The same foodstuff, beluga (white whale), uncooked and preserved in seal oil, was responsible for all 5 outbreaks. In 3 outbreaks Cl. botulinum, type E, was isolated, and it seems logical to assume that it was probably the factor in the other 2.

SURGERY

Treatment of Myocardial Infarction with Anticoagulants. B. V. Konyaev. Klin. med. 37:81-90 (March) 1959 (In Russian) [Moscow].

The author reports on 611 patients with myocardial infarction, 221 of whom were treated with anticoagulants and 390 without anticoagulants. Anticoagulants were given to patients with more extensive infarction frequently complicated with myocardial aneurysm and circulatory insufficiency. Mortality in the group treated with anticoagulants amounted to 7.2%; it was 11% in the control group. The incidence of thromboembolic complications was 10.8% in the first group and 13% in the second group. Treatment with anticoagulants was most effective in patients with recurring and extensive myocardial infarction complicated by circulatory insufficiency. However, the anticoagulant therapy does not prevent the development of extensive myocardial necrosis or of recurring infarction, especially in the presence of arteriosclerotic coronary vessels; nor does it prevent further extension of the existing infarction. There was not a more frequent formation of cardiac aneurysms and their rupture in the anticoagulant-treated group, despite the fact that the patients in this group were afflicted with a more severe pathological state.

The anticoagulants should be given at the earliest possible time so as to accomplish the lowering of prothrombin to 40-60% level as early as possible. Sudden termination of the anticoagulant treatment leads to thromboembolic complications, and for that reason it should be terminated gradually. Hemorrhagic complications in the group treated with anticoagulants amounted .to 16.6%. These hemorrhages were chiefly renal and were observed as mild hematuria.

The Coexistence of Primary Lung Cancer and Other Primary Malignant Neoplasms. C. G. Moertel, H. A. Andersen and A. H. Baggenstoss. Dis. Chest 35:343-347 (April) 1959 [Chicago].

Of 1,588 patients in whom a histological diagnosis of cancer of the lung was confirmed at the Mayo Clinic between 1944 and 1953, 65 (4.1%) had one or more other primary malignant neoplasms. Of the 65 patients, 59 were men and 6 were women. In 27 patients the lesions were diagnosed simultaneously; in 8 patients diagnosis of the pulmonary lesion preceded diagnosis of the other neoplasm by periods of 1 to 5 years; and in 30 patients diagnosis of the pulmonary lesion followed that of the other neoplasm by periods of 1 to 29 years (average 9.6 years). In 24 patients both lesions were diagnosed at operation only; in 8 patients both lesions were diagnosed at autopsy only; and in 33 patients one or more lesions were diagnosed both at operation and at autopsy. The distribution of the specific types of associated primary malignant neoplasms did not differ significantly from that expected in a comparable group of patients with single malignant neoplasms.

The reported data seem to establish definitely that the occurrence of an independent primary cancer of the lung in a patient with known malignant neoplastic disease at another site is not uncommon. Therefore, no solitary pulmonary lesion in a patient with a previously diagnosed cancer may be assumed to be metastatic without positive laboratory confirmation. In patients affording reasonable evidence that a primary malignancy elsewhere has been controlled, the presence of a discrete pulmonary lesion is an absolute indication for thoracotomy.

Ulcer of the Oesophagus. P. Rudström and B. Drettner. Acta chir. scandinav. 116:186-195 (no. 3) 1958-1959 (In English) [Stockholm].

The authors report on clinical pathophysiological and surgical observations made on 4 men and 4 women with solitary callous ulcer of the intrathoracic portion of the alimentary tract. The ages of the patients ranged between 37 and 75 years. The patients exhibited recurrent, severe retrosternal pain at the level of the lesion combined with a burning sensation and a feeling of obstruction to the passage of food. Dysphagia predominated, and the patients lost much weight. More than half of the 8 patients had a diaphragmatic herniation making possible reflux of the gastric contents. In 4 patients there was gastric or duodenal ulcer with marked symptoms, for which 2 of the patients had undergone an operation. In 2 patients gastric ulcer was combined with hiatus hernia. Contact between the mucous membrane of the esophagus and hydrochloric acid and pepsin from the stomach is believed to be a factor of great importance to the development of ulcerations. Therefore, surgical treatment was directed not only to removing the involved portion of the esophagus but also to resecting so large a portion of the stomach that the production of hydrochloric acid was almost entirely inhibited. Thoracotomy with resection of the 8th rib on the left side was performed. The cardial region and the lower esophagus were dissected free, and the fundus and body of the stomach as well as the lower portion of the esophagus were resected. The gastric stump was left as small as possible by means of resection of the lesser curvature in a distal direction. The proximal gastric incision was closed, and the esophagus anastomosed to the anterior wall of the stomach via a stoma. The anastomosis was secured with 2 layers of interrupted silk sutures. The suture line was covered posteriorly by the stomach and anteriorly by a flap of omentum. Despite the radical resection of the stomach, no obstruction to the passage of food was noted, nor were any nutritional difficulties recorded during the postoperative period. The majority of the patients gained weight rapidly. No serious postoperative complications occurred, and no deaths were recorded. The patients became immediately free of dysphagia, and their general condition showed rapid improvement. The results were found to be favorable on follow-up examination after an interval ranging from 1 to 7 years.

Pyloric Stenosis. J. A. Balint and M. P. Spence. Brit. M. J. 1:890-894 (April 4) 1959 [London].

The authors report on 86 men and 32 women with pyloric stenosis, defined as a condition in which obstruction to the emptying of the stomach is due to an organic lesion in the region of the pylorus. Of these 118 patients, the cause of the pyloric stenosis was established by laparotomy in 115, at autopsy in 2, and by roentgenographic examination in 1. A duodenal ulcer was the cause of stenosis in 95 patients. A gastric ulcer remote from the pylorus was the cause of obstruction in 7 patients. In 13 patients pyloric obstruction was due to carcinoma of the pyloric antrum; in 2 it was due to kinking of the duodenum which had become adherent to a chronically inflamed gallbladder; and in 1 it was due to a congenital diaphragmatic constriction at the pylorus. Vomiting attributable to pyloric stenosis occurred in all but 3 patients, being a presenting symptom in 105. A predominant pattern was discernible in 85 patients, with daily vomiting in 29, more frequent than daily in 35, and occasional in 21. Pain of ulcer type had occurred in 105 patients. Anorexia was present in 73 patients. Seventy-seven patients had lost 5 lb. (2.3 kg.) or more in weight. Diarrhea occurred in 23 patients (20%). It was usually slight, but in 6 it was severe enough to be a presenting symptom. The high incidence of offensive eructation in the patients with diarrhea suggests that stale food in the stomach leads to the production of some substance irritant to the intestine. The duration of obstructive symptoms before admission to hospital varied from one month in 37 patients to more than one year in only 14. Confirmatory physical signs associated with pyloric stenosis consisted of a gastric succussion splash in 66, of visible gastric peristalsis in 33, and of dehydration in 29. A barium-meal examination was performed on 93 patients and showed evidence of delayed emptying in 79. Anemia was common, and a raised hemoglobin level was rare. The blood urea level was raised to 50 mg. per 100 cc. or more in 50% of the patients.

The diagnosis of pyloric stenosis was reasonably certain when the following stringent major criteria were satisfied: a classic history of persistent vomiting of large amounts at times when the stomach should be empty, containing recognizable residues of food eaten some hours previously or accompanied by offensive eructation; the presence of visible gastric peristalsis; the main daily volume of the gastric residue exceeding 1,000 cc. on the first or last 3 days on which aspiration was performed; the stomach emptying by less than one-third in 2 hours, less than a half in 3 hours, or less than two-thirds in 4 hours, as estimated by the radiologist who performed the barium-meal examination. The definitive treatment was surgical in nearly all patients. There were only 2 deaths among the 92 patients operated on for pyloric stenosis due to a benign ulcer. By contrast, only 4 of the 13 patients with carcinoma left the hospital after a potential curative operation. Medical treatment, with repeated gastric aspiration or lavage, replacement of fluid and electrolyte loss, bed rest, and frequent milk feedings, although an essential preliminary to surgical treatment, was rarely tried as definitive therapy and never proved of lasting value.

Gastric Resection and Alcoholism. W. Dick, R. Fischer and G. Sautter. Deutsche med. Wchnschr. 84:311-316 (Feb. 20) 1959 (In German) [Stuttgart, Germany].

The authors point out that several years ago 2 Austrian investigators had found that every 5th inmate of a home for dipsomaniacs had undergone gastric resection, and thereafter others found even higher percentages. They then present the histories of patients from their own practice which had induced them to investigate the relationship between gastric resection and alcoholism. The authors gained the impression that from 2 to 3% of the patients who have undergone gastric resection are likely to become alcoholics to an extent that they require institutional treatment. They discuss alcohol addiction before operations on the stomach and studies on tolerance for alcohol and on alcohol resorption in patients who have undergone gastric resection.

If disease of the stomach and alcoholism have no connection, then the percentage of persons who have undergone gastric resection should be no higher in homes for alcoholics than in the general population. Exact information about this point is difficult to obtain. The investigators who first called attention to the high incidence of alcoholism in persons who had undergone gastric resection considered peptic ulcer and alcoholism as pathogenetically coordinated disturbances, pointing out that the same emotional conflict situations are found in ulcer patients and alcoholics. The 2 conditions are regarded as "equivalents," so that sometimes the ulcer patient will exchange the freedom from symptoms after the operation for alcoholism.

There is no doubt that gastric resection changes the mode of reaction to the consumption of alcohol. Improved "gastric" tolerance is accompanied by a "worsening" of "brain" tolerance for alcohol. This lack of tolerance may be responsible for the fact that some patients who have undergone gastric resection may be institutionalized for alcoholism, because, although they really are not drunkards, they had become intoxicated to a degree which would not have occurred if they still had an intact stomach. This factor of "reduced alcohol tolerance" should be impressed on patients who undergo resection and who drive motor vehicles, so as to prevent accidents. Commenting on the question whether alcoholism may lead to gastric resection, the authors say that this possibility is not remote. Alcoholism does lead to gastritis, but rarely to ulcer. Surgeons should be aware of an increased incidence of the sequels of alcoholism after gastric resection.

***Chronic Fibrous Mediastinitis and Superior Vena* Caval Obstruction Due to Histoplasmosis.** J. M. Salyer, H. N. Harrison, D. F. Winn and R. R. Taylor. Dis. Chest 35:364-377 (April) 1959 [Chicago].

The authors report on 3 men, between the ages of 25 and 30 years, and on a 30-year-old woman with bronchial or mediastinal venous obstruction due to chronic fibrous mediastinitis who were admitted to the Fitzsimons Army Hospital in Denver. The 4 patients underwent exploratory thoracotomy which revealed fibrous mediastinal lesions from which biopsy material was obtained. The lesions showed various degrees of calcification and were so extensive, obliterating anatomic planes, that pulmonary resections were technically impossible or considered unwise. In one patient the azygos vein and superior vena cava were excised, and the vena cava was replaced from the right innominate vein to the auricle by an aortic homograft. Clinical and laboratory findings with uniform gross and microscopic appearance of these intrathoracic lesions gave a sufficient basis to make a diagnosis of chronic fibrous mediastinitis due to histoplasmosis. Morphologically typical organisms of Histoplasma capsulatum were observed in the caseous material from a granulomatous lymph node in one patient, and organisms highly suggestive of such a fungus disease were found in the thick fibrous tissue obtained by biopsy from another patient. Proliferative collagenous replacement of lymph nodes renders histological and cultural confirmation of H. capsulatum difficult unless lymphoid tissue is obtained at thoracotomy before complete replacement of the granulomatous process with dense fibrous tissue. Buried within such lesions there may be found caseating granulomas which contain organisms typical of H. capsulatum. Multiple mediastinal biopsies from the other 2 patients were not conclusively diagnostic in that no lymph node showing such early collagenous replacement of necrotic foci was observed, although the typical hyalinized fibrous and calcific tissue was in abundance.

Other workers including clinicians, surgeons, and pathologists, who have reviewed the literature and their clinical experiences with chronic fibrous mediastinitis or obstruction of the superior vena cava, stated that from 15 to 50% of such lesions were secondary to chronic inflammatory diseases. Of the specific varieties, tuberculosis and syphilis always have been included or implicated. The authors suggest that a significant percentage of such lesions, considered in the past to be tuberculous, syphilitic, thrombotic, traumatic, rheumatic, cicatricial (keloid), or idiopathic in nature, were actually due to the rather uniform response of the mediastinal lymph nodes and related anatomic structures to infection with H. capsulatum.

Wound Irrigation to Prevent Local Recurrence of Cancer. R. G. Collier, R. C. Ey, G. O. McDonald and W. H. Cole. A. M. A. Arch. Surg. 78:528-534 (April) 1959 [Chicago].

The authors devised a biological animal screening procedure to assay the effectiveness of agents which could be used as wound irrigants to kill implanted cancer cells. Twelve such agents were tested in albino rats in which surgical wounds had been produced and inoculated with a cell suspension of the 256 Walker tumor. Among these agents was mechlorethamine, but it was tested only for comparison. The primary purpose of these experiments was to find a wound irrigant which was not a bone-marrow depressant. Such an irrigant could be used to irrigate the wound of a patient who also received mechlorethamine or a similar anticancer agent at the time of surgical intervention in the prophylactic or adjuvant program. A form of monoxychlorosene, Clorpactin XCB, was found to be the most effective non-bone-marrow depressing agent in preventing growth of tumors in the experimental animal screening procedure.

As a result of this study a clinical trial was started, a 1% solution of Clorpactin XCB being used to irrigate surgical wounds after radical mastectomies, radical neck dissections, and the perineal wounds of combined abdominoperineal resections. The wound is irrigated every 45 minutes during the operation with 250 cc. of a 1% solution of Clorpactin XCB made up in cool isotonic sodium chloride solution. The solution is allowed to remain in contact with the tissues for 3 minutes at each irrigation period. At the conclusion of the operation, just before the skin flaps are sutured, the wound again is irrigated with 500 cc. of the solution. The use of this wound irrigant should accompany adequate cancer surgery, and should not be construed as a replacement or a substitute for well-established and proved surgical procedures.

Hyperparathyroidism and Gastroduodenal Ulcer. J. Hellström. Acta chir. scandinav. 116:207-221 (no. 3) 1958-1959 (In English) [Stockholm].

The author evaluated the relation between hyperparathyroidism and peptic ulcer on the basis of data gathered from the literature as well as from personal observations on 121 patients with hyperparathyroidism. In 14 of the 121 patients (10 men and 4 women), a gastroduodenal ulcer was definitely present. The incidence of peptic ulcer was 28.6% in the men and 4.6% in the women. The age at which ulcer symptoms first appeared varied between 20 and 51 years. In most cases the ulcer symptoms started long before hyperparathyroidism was diagnosed. In all the 14 patients except one, the primary ulcer was in the duodenum. The pathoanatomic changes in the parathyroids consisted of a single adenoma in 13 patients and of primary hyperplasia of all the glands in 1 patient. Parathyroidectomy was performed on all 14 patients. In 10 patients the ulcer healed postoperatively; the condition of 3 patients improved and that of 1 remained unchanged.

Analysis of the data gathered from the literature and from the series of 121 patients revealed that the incidence of gastroduodenal peptic ulcer was greatly raised in patients with hyperparathyroidism. In some patients the relation between hyperparathyroidism and peptic ulcer was a coincidence. In other patients there was some relation between hyperparathyroidism and peptic ulcer, probably chiefly in the form of an unfavorable influence on healing of the ulcer. Finally, in some patients other endocrine factors, particularly in the form of ulcerogenic tumors of the pancreas, affect the development of peptic ulcer in patients with hyperparathyroidism.

Cancer of the Terminal Portion of the Large Intestine: Diagnostic and Therapeutic Aspects. J. Bastien, J. Boy and S. Segal. Strasbourg méd. 10:1-20 (Jan.) 1959 (In French) [Strasbourg, France].

The authors distinguish 3 types of cancer: small cancers whose dimensions do not exceed 2.5 cm., polypoid sessile tumor, and the most frequent type, infiltrating or stenosing ulcerated cancer for which radical treatment is indicated. Three aspects from cytological study of cells forming the neoplasm are the abundance of mitoses, the differences of density in chromatin from one cell to another, and finally the search for modifications of volume or number of nucleoli. These signs are absent in tumors of the villous type and in doubtful polyps. The following rules of conduct in treatment of cancer of the terminal portion of the large intestine were based on 121 cancers which the authors had treated: 1. For cancer beyond the possibility of surgical cure, only colostomy can be considered, completed by coagulation when it is possible. 2. A small tumor whose diameter does not exceed 2.5 cm. should be treated according to its high or low location by an abdominal resection alone or by radiotherapy with "contact doses." 3. Ulcerative cancer will have different therapy according to whether its seat permits conservation of the sphincter ani. All cancers below 12 cm. call for an abdominoperineal resection.

The authors paid particular attention to fast-developing cancer, and it is in order to lessen it that they employed definitive ileostomy and one or several sessions of contact radiotherapy. In more favorable cases contact radiotherapy alone was used in order to arrest progressing cancer. When the tumor is at the rectosigmoid angle or a little above it, it is removed by a resection performed by the abdominal route; this is preceded, when it is accepted, by a temporary colostomy.

The Experimental Development of Pseudomembranous Enterocolitis. T. L. Tan, C. T. Drake, M. J. Jacobson and J. van Prohaska. Surg. Gynec. & Obst. 108:415-420 (April) 1959 [Chicago].

Even though Staphylococcus pyogenes var. aureus has been isolated in most reported cases of pseudomembranous enterocolitis, there is still doubt about the cause of the disease, because obviously unrelating derangements of colonic flora have been reported in patients with the disease. The authors therefore reproduced enterocolitis in animals by a pure culture of Staph. aureus isolated from a patient with pseudomembranous enterocolitis. Chinchillas were used for the experimental studies, because they have been known to contract enterocolitis spontaneously after prolonged ingestion of certain antibiotics, particularly Aureomycin. When the inoculated chinchilla died, the same micro-organism was reisolated in pure culture from its intestine. In addition, the reisolated staphylococcus yielded enterotoxin poisonous to another animal. Thus, the experiment fulfills the 4 postulates of Koch. Strains of Staph. aureus isolated from patients with food poisoning or from those with pseudomembranous enterocolitis were tested. All these strains were capable of producing enterotoxin and were tested repeatedly for the content of enterotoxin.

The experiments were carried out on 12 chinchillas, which received their standard diet of cabbage, lettuce, and carrots. Cultures of their normal stools were obtained and sensitivity reactions to various antibiotics were determined. Guided by the sensitivity tests, the animals were given 50 mg. of oxytetracycline twice daily or mixtures containing 12.5 mg. of Aureomycin, 12.5 mg. of oxytetracycline, and 25 mg. of Gantrisin, or 12.5 mg. of oxytetracycline and 25 mg. of Gantrisin. The oral administration of this antibiotic mixture was maintained for 5 or more days. Beginning on the 6th day, the animals received a suspension of pure culture of Staph. aureus in 2 daily doses by mouth. In the first group of 3 animals the antibiotic mixture was continued along with the oral administration of the suspension of the micro-organism. In the second group of 2 animals the antibiotic was withdrawn on the 6th day, and from then on the animals received only the suspension of pure culture of staphylococcus. All experimental animals became sick. The untreated animals remained well. The principal symptoms were anorexia, lethargy, and occasional diarrhea. Particularly interesting observations were made on a third group of 3 chinchillas. They improved, but when they were retested after an interval, they died apparently as the result of the administration of the antibiotic, before the staphylococcus suspension was given. Explanations for this phenomenon are discussed.

The significant gross findings at autopsy were marked distention of the stomach, duodenum, and the entire small intestine. The principal microscopic changes observed were edema of the gastrointestinal tract, leukocytic infiltration of the mucosa, submucosa, and muscularis, superficial ulcerations, and passive congestion; in numerous segments the mucosa was completely sloughed off. In particular, the stomach showed leukocytic infiltration, thinning of the mucosa, and loss of the normal villous structures. The duodenum showed marked loss of mucosa with ulcerations, heavy leukocytic infiltrations, and fibrinomucous exudate or pseudomembrane in the lumen. The colon showed minimal microscopic changes, but even here one could discern changes compatible with inflammatory colitis. The authors conclude that the etiological agent of pseudomembranous enterocolitis is the enterotoxin-producing Staphylococcus organism.

Fractures of the Femoral Shaft in Children with Special Reference to Subsequent Overgrowth. B. Barfod and J. Christensen. Acta chir. scandinav. 116:235-250 (no. 3) 1958-1959 (In English) [Stockholm].

The authors report the results of a follow-up study on fractures of the femoral shaft in 126 children, under 15 years of age, treated at the Kommunehospital and the Amtssygehus in Aarhus, Denmark, between 1945 and 1954. Follow-up examinations were performed on 114 of the 126 patients, and the observation periods ranged from 2 to 12 years. Osteosynthesis was used for 23 patients and conservative treatment for 91. The duration of treatment was longer for those subjected to osteosynthesis than for those undergoing conservative treatment. Moreover, the patients who were treated conservatively had a better end-result in the form of a smaller inequality in the length of the fractured limb and an earlier return to normal gait than was seen in those treated with osteosynthesis.

Observations have shown that fracture of the femoral shaft in children is followed by a lengthening, which amounts to as much as 3 cm. after conservative treatment and often no more than 3 cm. after osteosynthesis. The lengthening occurring after conservative treatment seems to be compensatory in nature. Of the 91 patients in this series whose fractures were treated conservatively, about 80% showed normal length, with variations not exceeding plus or minus 1 cm., at the follow-up examination. After osteosynthesis, however, overgrowth always occurred as compared with the uninjured limb, and follow-up examination revealed lengthening in excess of 1 cm. in 20 of the 23 patients. A shortening of the fractured limb amounting to 2 cm. at the most, angulation of less than 25 degrees, and absence of rotation should be the aims of therapeutic measures which are carried out conservatively. Thus, osteosynthesis is not indicated in fractures of the femoral shaft in children.

New Points of View Concerning Pathogenesis of Dupuytren's Contracture. H. Millesi. Beitr. klin. Chir. 198:1-25 (no. 1) 1959 (In German) [Munich, Germany].

Observations on 231 patients with Dupuytren's contracture, who were operated on in the department of plastic surgery of the first surgical clinic of the University in Vienna, showed that the onset of the disease occurs frequently at an advanced age. Men are more often affected than women. The 4th and 5th fingers are involved most frequently. The contracture begins with a circumscribed thickening in the palm of the hand to which the skin is fixed. The course of the disease is characterized by bouts with prolonged spontaneous intervals of arrest. Histological examination of 11 embryonal and fetal pairs of hands in various stages, of 31 hands from cadavers, and of 41 surgical specimens obtained from patients operated on for Dupuytren's contracture showed that the connective tissue system of the palm is a functionally uniform body built up by a spatial connective-tissue network with deposits of fatty tissue and interspersed collagen fiber bundles in various directions. The contracture columns correspond to the course of the fiber systems. They represent, therefore, no new formations, but thickening of previously formed fiber bundles. Normally the individual fiber bundles possess microscopically a wave-like structure and contain elastic fibers.

The operative specimens obtained from 2 patients in whom the contracture was still in an early stage showed that, at the onset of the condition, a degeneration of the elastic fibers occurs and also thickening and hyalinization of the collagen fiber bundles. Only within the thickened fiber bundle proliferation of cells develops. An autogenous sensitization to degeneratively altered collagen is to be considered the cause of this proliferation. This concept was supported by the fact that the intracutaneous injection of a suspension of autogenous contracture tissue which was given to 14 patients caused a red papule in 10 patients; the subcutaneous injection of a suspension of homogenous contracture tissue which was given to 15 patients caused a similar reaction in 12. In contrast to that, this intracutaneous test gave negative results in control persons without Dupuytren's contracture. The proposed concept of pathogenesis of the contracture explains the occurrence of the contracture in the fiber bundles which are exposed to a pulling effect, and it also explains the fact that finger contracture, which has become established, becomes worse if mechanical extension exercises are carried out for therapeutic purposes.

Synthetic Materials as Vascular Prostheses: III. Long Term Studies on Grafts of Nylon, Dacron, Orlon, and Teflon Replacing Large Blood Vessels. J. H. Harrison. Surg. Gynec. & Obst. 108:433-438 (April) 1959 [Chicago].

In a comparative study of synthetic materials as vascular prostheses under various conditions, grafts of nylon, Dacron, Orlon, Teflon, and Ivalon Sponge were inserted into defects created in the thoracic aortas of 84 dogs. The results with these after 1 or 2 years have been previously reported. There was rapid breakdown of the Ivalon Sponge, leading to aneurysms and rupture of the grafts. Nylon lost 80% of its original strength by 6 months and up to 95% after 2 years. No complications were encountered with grafts of Orlon, Dacron, or Teflon after one year, and the materials lost little of their original strength. In this paper the author presents observations on 10 of the original group of 84 dogs observed for periods up to 3 years.

Maintenance of patency was no problem, as only one graft became occluded and this secondary to a hematoma. There was delayed bleeding through the interstices of grafts of nylon, Dacron, and Orlon resulting in encapsulated hematomas. Nylon continued to lose strength. Complete breakdown resulted with rupture in 2 grafts. Dacron, Orlon, and Teflon maintained most of their strength during the period of observation. Grafts made of Teflon were the only ones in which complications did not occur when observed for 2 years. In addition, Teflon should, due to its greater chemical inertness, be expected to maintain its strength over a longer period of time. It is considered the synthetic material of choice as a vascular prosthesis and superior to homografts for replacing vessels larger than 9 mm. in diameter.

Left-sided Pneumatosis Coli. C. A. Neumeister. Minnesota Med. 42:407-408 (April) 1959 [St. Paul].

The author reports the case of a 49-year-old woman with intestinal pneumatosis, a rare condition of unknown causation which is now becoming more generally recognized. The patient complained of abdominal distress of an aching type. Sigmoidoscopic examination revealed what appeared to be multiple polypoid lesions beginning at the 8-cm. level. Barium-enema studies revealed multiple polyps throughout the descending and the sigmoid colon. At laparotomy and colotomy no polyps were found, and the diagnosis of left-sided pneumatosis was definitely established. Two months after the surgical intervention sigmoidoscopic examination revealed almost complete disappearance of the intramural cysts. The patient was asymptomatic.

The pathological picture is best explained by the theory that gas distending the lymphatics with blockage of the lymphatics causes the cystic distention in the submucous and subserous layers of the intestine. The composition of the gas in the cysts has apparently never been determined. The inflammatory reaction surrounding the cysts varies from the acute type with leukocytic infiltration to granulomatous changes with epithelioid cells and giant cells of the multinucleated type. Of the concepts proposed as to the causation of pneumatosis, the nutritional deficiency theory is the only one supported by experimental evidence. The syndrome is self-limited and does not require any specific treatment unless complications supervene. Once the diagnosis of pneumatosis is made, the treatment is expectant, and one can expect spontaneous remission.

NEUROLOGY & PSYCHIATRY

Course of Spinal Amyotrophy of Childhood. D. Furtado. Arq. pat. 30:522-532 (Nov.) 1958 (In Portuguese) [Palhava, Lisbon].

According to the classical conception, spinal amyotrophy of the Werding-Hoffmann type begins in early life and ends fatally in from a few months to 4 years. It is a type of familial and progressive disease. A case of the disease compatible with life of the patient and with regression of paralysis is reported. The patient was normal up to the age of one year, when he already walked by himself. Paralysis appeared at that age and became acute. The child was observed for the first time at the age of 2 years with complete paralysis, amyotonia, and amyotrophy. Cephaloplegia was complete, although the facial muscles were normal and talking and swallowing were normal. Respiration was of the abdominal type. Biopsy and electromyograms showed changes of progressive spinal amyotrophy. The patient was able to move only the hands and feet.

The patient's parents were first cousins. Some members of the family had neuropathic disorders, but an older sister was normal. The patient was observed for 12 years, up to the age of 14. Early diseases of childhood and infections were controlled with antibiotics and sulfanilamides. The treatment for the muscular disease consisted of mild physical therapy, with passive movements and stimulation of active movements. A slow but constant regression of paralysis of certain muscles became evident between the ages of 5 and 12 years; this became a frank regression between the ages of 12 and 14 years. The patient is now able to swim the span of a pond unaided. He can be seated in a chair and is able to write and to feed himself. Somatic and sexual development is normal. The intelligence quotient is normal, and the patient today is an advanced student in high school.

The author points out that the prognosis of progressive spinal amyotrophy depends on the form, either typical (severe) or benign. A frank regression of paralysis and indefinite prolongation of the life span correspond to the benign form of the disease. This was the form in the case reported.

Circumscribed Cerebral Thrombophlebitis. G. Dalle Ore and R. Da Pian. Minerva med. 50:519-526 (Feb. 21) 1959 (In Italian) [Turin, Italy].

The authors discuss the clinical picture of acute circumscribed cerebral thrombophlebitis terminating in a complete remission in 2 boys, 9 and 10 years of age. The disease was attributed to the exacerbation of a mild, chronic otitis. A pain more intense than usual developed in the affected ear of each boy 20 and 15 days, respectively, before admission. An episode of intense headache, accompanied by unmanageable vomiting and followed by fever, convulsive seizures, motor and speech deficiency, and coma, took place in both patients 2 and 3 days, respectively, before admission. This state persisted for 2 or 3 days. The disease resolved gradually and slowly in one patient, and rapidly in the other, after the patients had received a high-dosage treatment of specific antibiotics and systemic drugs. The recovery was complete in both patients, without any neurological sequelae, and they were discharged on the 40th hospital day.

The electroencephalograms of both patients were obtained while the neurological symptoms were subsiding. The pathological changes recorded by electroencephalography involved both hemispheres in one boy and the affected hemisphere only in the other. These changes, although in less degree, were also observable on the 30th hospital day. Arteriographic findings were negative except for a slight displacement of the anterior cerebral artery on the frontal plane in one patient and the enlargement of venous vessels in the other. Spinal canal puncture revealed no abnormality in one boy and only a slight increase of white blood cells in the other. Examination of the fundus oculi was negative in both patients except for enlargement of the veins. Despite the absence of any neurological lesion, the correct diagnosis was made in the patient who was first hospitalized during resolution of the disease. The correct diagnosis in the patient who was subsequently hospitalized was easier and was made more promptly, because the neurological symptoms were subsiding at the time of admission and in view of the acquired experience with the first patient.

Poliomyelitis in the Sudan. M. A. Haseeb. J. Trop. Med. 62:45-46 (Feb.) 1959 [London].

The author believes that the immunological status of a population should be assessed before decisions are made as to whether vaccination against poliomyelitis should be carried out or not, and if so to what extent. In the absence of reliable statistics, useful data may in certain circumstances be obtained from serologic surveys. This communication is concerned with the results of serologic tests performed on 2 groups of Sudanese children. One group consisted of 48 children from the rural region of Kassala, and the other group consisted of 46 children from the urban area of Khartoum. The children ranged in age from 18 months to 14 years. All serums neutralized 1, 2, or all 3 types of poliomyelitis virus. The pattern of poliomyelitis in the Sudan conforms with that prevailing in the countries of Africa previously studied. The incidence is high early in life, but the morbidity is low, and the disease seldom ends fatally. The author concludes that mass vaccination against poliomyelitis is not indicated at present in the Sudan.

Investigation of Families with Two or More Mentally Defective Siblings: Clinical Observations. S. W. Wright, G. Tarjan, and L. Eyer. A. M. A. J. Dis. Child. 97:445-463 (April) 1959 [Chicago].

Several genetically determined biochemical abnormalities, such as phenylketonuria and aminoaciduria, associated with mental defect have been described by other authors in siblings. These observations suggest that among members of families with 2 or more defective siblings the likelihood is high that there are some persons with an inherited biochemical defect. In an attempt to prove this concept, the authors carried out a study at the Pacific State Hospital, an institution for the mentally defective in Pomona, Calif., in which 61 families with 2 or more mentally defective siblings were identified. Clinical observations on the siblings and their parents are reported; special biochemical observations will be the subject of a later report. There were 319 siblings in the 61 families. Of the 319 siblings, 107 were of normal mentality; the intellectual status was unknown in 23, and in 28 the mental status was subnormal; 13 siblings were known to be mentally defective but had not been institutionalized; and the remaining 148 siblings had a mental defect for which they had been institutionalized. The groups of defective siblings ranged from one in which the defective siblings had intelligence quotients of 87 and 71, respectively, to one with 3 siblings with a heredodegenerative disorder and intelligence quotients below 5. In 14 families there were defective twins; 13 sets were of the same sex, and 1 set was mixed.

Of the 319 siblings, 185 were males, of whom 108 (57%) were defective, and 134 were females, of whom 53 (47%) were defective. The 2:1 ratio of males to females in this group is significantly higher than the 3:2 male to female ratio in the over-all hospital population. There were 26 families with only males affected; 15 of these had normal female siblings. In 6 families only females were defective, and in the remaining 29 families there were both male and female defective patients. Over 50% of the fathers and mothers had evidence of inadequate intellectual status or disturbed social behavior with or without institutionalization.

Disorders with a known biochemical abnormality were found in 5 families. These included 4 defective sibling groups with phenylketonuria and 1 with lipochondrodystrophy (gargoylism). Among the remaining 56 groups, significant somatic, neuropathological, and psychopathological findings were noted in 7 families. It is possible that a simple type of inheritance may account for the mental defect in some of these groups. They included individual groups with ectodermal dysplasia (hypotrichosis), true microcephaly, congenital cataracts, Roussy-Lévy syndrome (a variant of Friedreich's disease), heredodegenerative disorder, schizophrenic symptomatology, and a possible sex-linked disorder with severe mental defect. A definite clinical diagnosis was made in 5 additional groups. They included 2 groups with Mongolism and 2 with prematurity and retrolental fibroplasia; in the 5th group one sibling was defective as a result of postnatal infection and the other as a result of severe trauma. This "defective sibling" method appears to be of value in isolating for further study a group of patients with an increased likelihood of a genetically determined biochemical disorder.

Serological Studies of the Poliomyelitis Epidemic in Huskerville, Neb. W. E. Engelhard and P. M. Bancroft. A. M. A. J. Dis. Child. 97:409-417 (April) 1959 [Chicago].

An abrupt, severe outbreak of poliomyelitis, which occurred in Huskerville, Neb., in 1952, was reported by the authors in a previous paper in The Journal, June 22, 1957, page 836. This epidemic of poliomyelitis was explosive, running its course in 5 weeks with 20 confirmed clinical paralytic cases and 31 nonparalytic cases among a population of 1,142 persons. The present report describes the distribution of types 1, 2, and 3 poliomyelitis neutralizing antibodies in the serums of Huskerville residents, who had had paralytic and nonparalytic symptoms in the course of the 1952 epidemic, and in the serums of 270 children in Huskerville, who did not have clinical poliomyelitis in 1952 and served as controls. The serologic findings showed the causative agent to be type 1 virus. Type 1 virus was not restricted in its distribution to the high-incidence area but was disseminated throughout the community. The incidence of involvement was greater in the area of high incidence of clinical disease.

Distribution of poliomyelitis viruses in the post-epidemic control group, consisting of children, between the ages of 6 months and 13 years, who moved into Huskerville 12 to 18 months after the epidemic, followed the usual pattern. Neutralizing antibodies were absent in the younger age group, while they appeared with increasing frequency in succeeding age groups. Observations, when compared with the control group of epidemic exposure on antibody levels, showed marked increase of type 1, moderate increase of type 2, and little change of type 3 antibodies. High-titer poliomyelitis neutralizing antibodies were shown 2 years after the epidemic. No differences in immune response were observed among paralytic and nonparalytic cases. However, type 1 virus proved to be the most antigenic. Very limited findings suggest the absence of cross immunity with the 3 types of poliomyelitis, and ability to produce neutralizing viral antibodies seems to develop with age.

GYNECOLOGY & OBSTETRICS

Abdominal Cesarean Section for Previous Tumor Constituted by Malformation of Uterus. M. R. Giron. Rev. españ. obst. y ginec. 15:342-344 (Nov.-Dec.) 1958 (In Spanish) [Valencia, Spain].

A 33-year-old woman was hospitalized at full term of her third pregnancy. She had previously had 2 children, now 7 and 4 years old, respectively, who were delivered normally. On hospitalization the patient had regular contractions every 2 minutes, lasting for 20 or 30 seconds. The fetal heart beat was normal, and palpation revealed that the fetus presented normally. The neck of the uterus was dilated 2 cm., but it was pushed toward the back of the pubis by a tumor located in the Douglas cul-de-sac. The tumor could not be mobilized, and it prevented engagement of the fetal head. Cesarean section was accordingly performed, after which it was observed that the tumor could be moved out from the cul-de-sac. The supposed tumor proved to be the part of a double uterus which during pregnancy folded behind the pregnant part, occupied the Douglas cul-de-sac, and acted as if it were a growth, causing dystocia. Both parts of the uterus were left undisturbed in the belief that, when their anatomic relationship would have been reestablished, the uterus would appear as made up of 2 symmetrical horns, divided by a slight partition and having a common neck. Both halves of the uterus were of the same size and capacity. Which one had been occupied by the fetuses in the 2 previous deliveries was unknown.

Smears, Colposcopy, Biopsies in the Early Diagnosis of Cancer of the Uterine Cervix on the Basis of 892 Cases. J. Mathieu and P. Villedieu. Lyon chir. 55:25-35 (Jan.) 1959 (In French) [Paris].

The results obtained by colposcopy and vaginal cytological studies in 892 patients between September, 1955, and November, 1957, have been analyzed in an attempt to determine the value of these procedures in the early diagnosis of cervical cancer. The clinical course of the patient, which is the only absolute criterion of accuracy, was used in evaluating the findings. Study of 638 vaginal smears yielded 18 false-positive or false-negative readings, or a percentage of error of 2.8%. Only 10 errors were recorded in 1,178 colposcopies, making a much smaller percentage of error. The simultaneous use of both methods, which the authors advocate, has proved accurate as judged by the clinical course in every case but one, that of a patient with an endocervical neoplasm who had previously been given radium treatment in an unknown dosage. The patient refused further radium therapy, which was advised because of a suggestive smear, and was later found to have a neoplasm of the isthmus.

The biopsy findings were never inconsistent with the later course. The comparatively small number of biopsies (171) in this series reflects the authors' increasing confidence in the reliability of the findings obtained by simultaneous study of the vaginal cytology and colposcopy. Biopsy is resorted to without delay, however, when the colposcopic findings are doubtful or when the clinical picture is at variance with the results of the investigative procedures.

Another aspect of the question of early diagnosis of cervical cancer is the problem posed by epithelioma in situ and its treatment. The authors have been much more impressed by the risk of true invasive cancer at some distance from the area from which the biopsy specimens are obtained and by the frequency of secondary degeneration in the cervix after local treatment than by certain figures published in the literature that seem favorable to the regression and propitious course of neoplasms in situ treated locally. They, therefore, believe that hysterectomy is advisable in patients in the neighborhood of the menopause. Greater circumspection and a more conservative attitude seem, however, to be warranted at present in regard to the findings in younger women.

Hazards of Abdominal Roentgenograms in Pregnant Women: How to Reduce the Risk of Irradiation to the Fetus During Radiopelvimetry? P. Magnin. Presse méd. 67:254-256 (Feb. 7) 1959 (In French) [Paris].

A study carried out by Miss Stewart and co-workers in Great Britain between 1953 and 1955 showed that of 1,500 children, aged less than 10 years, who died of leukemia and of malignant tumors, a large number had been subjected to irradiation in utero during radiopelvimetry of the mother. The proportion of children thus irradiated was nearly twice as great as that found in a rigidly selected control group. The hazard seemed to be 3 times as great when the abdominal roentgenograms were made in the first half of pregnancy as it was when they were made later, and the risk seemed to increase in proportion to the number of exposures.

The legitimate use of radiopelvimetry is not questioned because, among 1,000 pregnant women on whom abdominal roentgenography was performed in France, not one case of leukemia or of malignant disease occurred which could be attributed to radiation. The author believes that the risk of not recognizing a pelvic narrowing has much graver consequences than radiopelvimetry. Precautions should be taken to reduce to a minimum the radiation hazards to the fetus while performing radiopelvimetry on the mother. Abdominal roentgenography should not be performed at the beginning, but only during the last weeks of pregnancy when the relationship of the fetal head to the maternal pelvis can be demonstrated. The author shows by diagrams that the amount of exposure of the fetus depends greatly on the position of the mother during radiopelvimetry, a fact which is borne out by previously published measurements by other investigators.

PEDIATRICS

Electroencephalographic Study of Tuberculous Meningitis in Children, Particularly of Those Treated Only with Isoniazid. A. Colarizi and G. Canova. Helvet. paediat. acta 13:204-217 (Aug.) 1958 (In French) [Basel, Switzerland].

The authors report clinical and electroencephalographic studies on 17 children with tuberculous meningitis, who were treated only with isoniazid in doses ranging from 15 to 30 mg. per kilogram of body weight daily. The drug was usually given by mouth. In only 3 of the children was it also given during the first few weeks by the intraspinal route. Three of the 17 children died during the first few days, but the other 14 survived without neuropsychiatric sequels. Clinical cure and normalization of the electroencephalogram were more rapid and more complete in children treated only with isoniazid than in a comparable group treated earlier with streptomycin, which was usually given by intraspinal injection, alone or with other drugs. Only 2 of the 14 surviving children treated with isoniazid still showed slight electroencephalographic changes from 2 to 4 years after the onset of the tuberculous meningitis, whereas follow-up studies on 18 children who before 1953 were treated with streptomycin plus aminosalicylic acid revealed that 5 still had neuropsychiatric and 15 still had electroencephalographic disturbances.

Psychological and Somatological Examinations on Children After Tuberculous Meningitis. E. G. Huber. Helvet. paediat. acta 13:218-227 (Aug.) 1958 (In German) [Basel, Switzerland].

The author reports the results of psychological and physiological examinations on 33 children who had survived after tuberculous meningitis. Twenty-six of the children were the survivors of the 37 children treated for tuberculous meningitis at the author's clinic between 1950 and 1956; the other 7 had been treated elsewhere. The majority of the children had had tuberculous meningitis more than 5 years before, and a minimum period of 18 months had elapsed for all of them. The results of the physical examinations with regard to changes in the eyegrounds, to lesions of the cochlear and vestibular nerves, to hemiplegia, etc., corresponded largely to those reported in similar cases by other investigators. Intracranial calcifications were found not only in the severely damaged children but also in 2 children who showed no residual defects. Likewise, there was no correlation between the electroencephalographic findings and the severity of the meningitis process. All the children with somatic lesions also showed psychological deviations and derangements.

Even the 24 children who apparently had completely recovered from tuberculous meningitis had more or less severe disturbances of the autonomic nervous system and of affectivity and had some intellectual defects, as well as neuropathic and neurotic symptoms. Behavioral disturbances ranged from pronounced instability to complete lack of self-control and destruction of personality. Despite normal intelligence, many children showed a diminished power of concentration and association; some of them showed hereditary traits in the form of an exaggerated caricature. Because there seems to be a correlation between the degree of psychological disturbance and the loss of consciousness during the acute phase of the disease, the organic origin of the psychological disturbances is demonstrated, and it is possible to make a prognosis during the acute phase. It is proposed that, in order to avert the severe disturbances after tuberculous meningitis, the patient should receive mental hygiene guidance.

Problem of Enuresis: Psychopathological and Urologic Studies on a Fairly Large Series of Patients with Enuresis. A. Weber and N. Genton. Helvet. paediat. acta 13:275-291 (Oct.) 1958 (In German, with the Urologic Study in French) [Basel, Switzerland].

The authors define the term "enuresis" as uncontrolled passage of urine occurring during day and night in children over 4 years of age, most of whom also are able of normal micturition and can manage to stay dry for shorter or longer periods. Of 73 boys and 27 girls with enuresis who attended the pediatric clinic of the University in Zurich, Switzerland, 50 were subjected to a combined psychological and somatic study, and the other 50 were studied somatically only. Psychopathologically, these children with enuresis were subdivided into 4 groups as follows: 27 children with psychoreactive disturbances, 9 children who had remained infantile mentally, 4 children with organic cerebral impairment, and 8 children who were mentally normal. Two children were doubtful borderline cases. The somatic study included cystometry and urethrography in the course of micturition, in addition to general-clinical and neurological examinations. From the somatic point of view these patients were subdivided into 3 groups as follows: 17 children who were physically normal, 18 children with a functional disturbance of the bladder, and 15 children with organic changes in the genitourinary tract.

Three conclusions were drawn from these observations: 1. Enuresis may be organically conditioned in 33% of the children, which is a higher incidence than has generally been assumed. 2. Of the 27 children with a psychoreactive disturbance, 15 were somatically normal, 6 had functional disturbances, and 6 had organic impairment; these data suggest that, if the psychological examination of a patient with enuresis reveals a psychic disturbance, the enuresis must not necessarily be a symptom of this disturbance. 3. A somatic cause of the enuresis may be considered with a high degree of probability in those patients with enuresis who were found to be mentally normal. Of 8 mentally normal children with enuresis, 6 had organic impairment, and 2 had a functional disturbance. Concerning treatment, psychotherapy, in the widest sense of the term, is recommended for patients with a psychoreactive disturbance. Causal treatment is not available for children with constitutional infantilism, but symptomatic treatment with parasympathicolytic agents may be effective in some of these patients. Teaching of rhythmics in order to increase the capability for the formation of conditioned reflexes is recommended as a "method of neurological training" for children with enuresis due to organic cerebral impairment; in older children this may be combined with education aimed at calling the children's particular attention to the motor control of the bladder. Therapy must, therefore, be differentiated depending on the causation of the enuresis as revealed by combined psychological and somatic studies.

Attitude Study of Parents with Mentally Retarded Children: I. Evaluation of Parental Satisfaction with the Medical Care of a Retarded Child. R. Koch, B. V. Graliker, R. Sands and A. H. Parmelee Sr. Pediatrics 23:582-584 (March) 1959 [Springfield, Ill.].

Data about the attitudes of the parents of retarded children toward the pediatrician and the general practitioner, related specifically to diagnosis, care, and counseling concerning mental retardation, were obtained from 105 families by the clinic for the study of mental retardation at the Los Angeles Childrens Hospital. Eighty of 105 families were seen by either a pediatrician or a general practitioner; 14 were seen by a pediatrician and a general practitioner; and the retarded children of the remaining 11 families were cared for in well-baby clinics or in the outpatient department of the Childrens Hospital. Only retarded children less than one year of age at the time of referral were accepted for study.

Forty-seven per cent of the parents were satisfied with the care of the pediatrician as compared with 55% of the parents satisfied with the care of the general practitioner. The parents of 8 of the 14 children seen by a pediatrician and a general practitioner were dissatisfied with both. Five other parents in the group seen by both physicians were critical of the pediatrician but satisfied with the general practitioner, and only one parent was critical of the general practitioner but satisfied with the pediatrician. Complaints most frequently voiced regarding the pediatrician were: "He was too rushed"; "The examination was not thorough"; "Not interested in the child"; "We weren't told anything"; and "Seemed hesitant to make the diagnosis." In other cases, when a diagnosis was made, the parents felt that the pediatrician was "too blunt," "rushed us into placement," "was unfair in predicting the future," or "emphasized the effect on our other children." Criticisms expressed toward the general practitioner were essentially the same. The criticisms of medical care can thus be divided into 2 groups, namely, criticisms of what the parents were told and criticisms of how they were told.

The recorded data show that parents of retarded children frequently take their child to various physicians without satisfaction. This is probably, in large measure, due to the fact that many physicians are not well trained to cope with the problem of retardation in early infancy. The findings in this study may be related to the general practitioner's better understanding of the family, which enables him to deal more effectively with parents. Failure of the pediatrician may be due to a lack of adequate training in the field of mental retardation.

As a result of these studies, the curriculum of the department of pediatrics of the University of Southern California school of medicine has been changed to include 4 3-hour sessions concerning the problems of mental retardation. Didactic lectures have also been organized for the nursing and resident staff at the Los Angeles Childrens Hospital. Mental retardation is a subject which needs serious consideration by pediatric educators.

Familial Lymphopenia Associated with Agammaglobulinemia and Severe Moniliasis: The "Essential Lymphocytophthisis" as a Particular Form of Agammaglobulinemia of Early Infancy. R. Tobler and H. Cottier. Helvet. paediat. acta 13:313-338 (Oct.) 1958 (In German) [Basel, Switzerland].

In 1950 Glanzmann and Riniker described for the first time in 2 nursing infants, a 4-month-old girl and a 5-month-old boy, each from a different family, the aspect of a disease which is characterized by a frequent familial occurrence of an extreme lymphocyte deficiency in the peripheral blood and in the lymphatic organs, and for which the term "essential lymphocytophthisis" was proposed. The authors studied 2 siblings of the infants reported on by Glanzmann and Riniker, a 6-month-old boy (the brother of the first reported girl) and a 2½-month-old boy (the brother of the first reported boy). The absolute number of lymphocytes in all 4 children was below 1,000 in contrast to numbers varying from 5,000 to 6,000 normally observed in infants of these ages. At birth all 4 infants appeared to be healthy and strong nurslings, and the onset of the disease occurred after a few months with a mild but refractory thrush infection in the oral cavity. Later, more or less severe gastrointestinal disturbances and acute suppurative disorders, such as subcutaneous abscess, otitis media, dacryocystitis, suppurative rhinitis, and pyoderma, occurred. At the age of 2 to 6 months the disease aspect became more severe, and up to the patients' deaths, at the ages of 3½ to 7 months, a severe moniliasis with septic temperature curves and signs of bronchopneumonia predominated. In 3 of the 4 infants a generalized morbilliform rash occurred at the height of the disease. The erythrocyte sedimentation rate was only moderately increased in all the patients.

In the 2½-month-boy, the infant who was examined last, laboratory tests revealed a syndrome of lack of antibody formation with agammaglobulinemia; it seems probable that the same defect was present in the other infants. The authors do not consider the extreme lymphocyte deficiency as "phthisis," i. e., a secondary atrophy of a previously normally developed lymphatic tissue, but they tend to consider it as a primary disturbance of formation and function of the lymphoreticular apparatus. Consequently, they prefer the term "familial lymphopenia" to that of "essential lymphocytophthisis." The familial lymphopenia with agammaglobulinemia represents a particular form of agammaglobulinemia of early infancy, which differs from the previously known familial agammaglobulinemia (Bruton) by the fact that girls may also be affected and by the simultaneous occurrence of extreme lymphocyte deficiency. It could be due to a more pronounced defect of formation and function of the lymphatic tissue than that occurring in patients with common familial agammaglobulinemia. The lymphocytic as well as the plasmocytic series are deeply affected. The severe mycotic infection is the result of the disturbed defense power against infection.

Transitory Agammaglobulinemia of Early Infancy: Delayed Occurrence of Gamma Globulins and Specific Beta-2 Globulins. R. Tobler. Helvet. paediat. acta 13:339-346 (Oct.) 1958 (In German) [Basel, Switzerland].

The author reports on a 12-month-old infant who was hospitalized for several attacks of pharyngitis with high fever, morbilliform rash, swelling of cervical lymph nodes, enlargement of liver and spleen, and edema of face, hands, and feet. After 2 months of hospitalization the infant was discharged, and at the age of 18 months he again had 2 attacks of fever with erythroderma and edema of feet and hands. Serologic studies were done shortly after the patient's admission to hospital with the aid of paper electrophoresis which revealed complete absence of gamma globulins; the antiglobulin inhibition test showed that the gamma globulins were reduced to about 60 mg. per 100 cc., a value which was considerably lower than that to be expected normally (450 mg. per 100 cc.) at this age. Isoagglutinins could not be detected. Up to the age of 14 months, the infant thus presented the clinical picture of agammaglobulinemia with lack of antibodies. While in the hospital, he was treated for a short period with tetracycline (Achromycin), and on the day of discharge he was given an intramuscular injection of 10 cc. of gamma globulin.

The patient was followed up for 7 months after his discharge. Serologic studies repeated at 3-month and 7-month intervals revealed a delayed appearance of gamma globulins and beta-2A and beta-2M globulins. The patient was given 2 additional gamma globulin injections 1 month and 7 months after his discharge. The reported observations proved again that the diagnosis "agammaglobulinemia with lack of antibodies" in nursing infants can only be made when the child has been observed for a sufficient length of time, since this condition can easily be mistaken for the physiological hypogammaglobulinemia present at this age, and particularly for the transitory agammaglobulinemia of early infancy.

Chronic Lead Poisoning: A Review of Seven Years' Experience at the Children's Hospital, District of Columbia. G. J. Cohen and W. E. Ahrens. J. Pediat. 54:271-284 (March) 1959 [St. Louis].

The authors report on 43 children with chronic lead poisoning, who were admitted to the Children's Hospital in Washington, D. C., during the period from 1950 through 1956. Most of the children were between the ages of 1 and 3 years. Of the 43 patients, the cases of 38 were diagnosed during the months of May through October. No cases of acute lead poisoning, such as are caused by inhalation of lead fumes, have been observed. Twelve of the 43 children were asymptomatic, 14 presented clinical symptoms without encephalitis, while 8 demonstrated mild and 9 severe encephalitis. The asymptomatic patients were children who had no apparent sign or symptom of lead intoxication, but, during study of families of patients with plumbism or during study for other symptoms, these children were discovered to have a significant accumulation of lead within their bodies. The patients with simple lead intoxication had anemia and gastrointestinal complaints, such as cramps or constipation. The patients with severe encephalitis had prolonged convulsions or coma for as long as 24 to 48 hours, while the patients with mild encephalitis had central nervous symptoms and signs not including those of severe encephalitis. Six of the 43 patients had marked pallor on admission, which focused attention on the hematopoietic system. An observation that deserves particular emphasis was the absence of lead lines on the gums in all the patients.

When a history of pica is sought in children with chronic lead poisoning, it is almost always found. Forty of the 43 patients had a positive history of pica. Siblings of 18 children and mothers of 4 children also demonstrated pica. Pica in these children resembled an addiction and was usually selective for a particular substance. In contrast, indiscriminate pica was seen in this series only in children with severe brain damage. The 2 most helpful diagnostic procedures, other than lead determinations, were hematological and roentgenologic studies. Hematological studies on admission were abnormal in 37 of the 43 patients. Thirty-five children presented anemia, 29 basophilic stippling, and 23 eosinophilia. It is interesting to note that not all the children with lead poisoning showed stippled red blood cells; of those who did, one-third showed stippled red blood cells only after repeated smears were examined. Roentgenologic studies revealed increased metaphysial densities suggestive of lead poisoning in 34 of 37 long bone roentgenograms, in 1 chest roentgenogram, in 1 pelvic roentgenogram, and in 4 skull roentgenograms.

This group of 43 patients was treated with ethylenediaminetetraacetic acid (EDTA) administered either intravenously or subcutaneously in the standard dose of 30 mg. per kilogram. It is believed that EDTA combines with lead only in body fluids and soft tissues; a rest period between courses of treatment has, therefore, been suggested to allow the lead in the bone to reestablish equilibrium with the lead-depleted soft tissues. Thus, EDTA was given for 5 days, withdrawn for 3 days, and then repeated for 5 days. No evidence of local or systemic toxicity from EDTA has been noted. In general, treatment has been dictated by the clinical status of the individual, since the results of the chemical studies for lead were usually not reported for 1 or 2 weeks and then frequently did not correlate well with the severity of the symptoms. Intensive supportive nursing care, parenterally administered anticonvulsants, restricted fluids, and EDTA have been the mainstays of therapy.

Three of the 43 children died (all with severe encephalopathy) after an average of 2⅓ days of hospitalization. Eleven of the patients have been lost to follow-up. Of the remaining 29 patients, 16 are considered well, 5 present moderate residuals, and 8 have severe residuals. The high incidence of residuals (45%) of neurological and psychiatric nature deserves serious consideration. It is suggested that counseling directed at cessation of pica seems to be an effective tool in prevention of continued lead poisoning. Perhaps even more important are the roles of private physicians and public health authorities in preventing the occurrence of this dangerous disease through education of the public, inspection and proper repair of substandard housing, and more stringent laws regarding lead-containing paints.

Infantile Spasms and Hypsarrhythmia. B. D. Bower and P. M. Jeavons. Lancet 1:605-609 (March 21) 1959 [London].

The authors report on 22 infants, between the ages of 1 and 17 months, with spasms, who attended the Children's Hospital in Birmingham, England, between January, 1955, and December, 1957. All the patients except one had had the first spasm before the age of 10 months, and in 14 it occurred between 4 and 8 months. There were 15 patients with flexor spasms and 7 with extensor spasms as the presenting feature. The spasms were generalized, rapid, and brief. In some patients the spasm was followed by a cry, and it was often repeated to form a series. Definite mental retardation, often severe, was almost invariably associated with the spasms. In 11 patients there was a history of prenatal or perinatal cerebral damage, and the mental development was usually retarded from birth; physical abnormalities were found in 8 of these patients. In the remaining 11 patients the causation of the spasms was unknown, and in these children mental development was usually normal up to the time of the first spasm. Routine anticonvulsant therapy was disappointing. Chlortetracycline produced a temporary remission or reduction in the number of spasms in 5 patients, and in 1 other patient the remission was permanent; the latter was the only patient who showed mental improvement after the drugs administration. One patient died at home at the early age of 2 years and 9 months. Most of the survivors remained pathetically unchanged as idiots or imbeciles.

The electroencephalographic recordings of the patients with infantile spasms were almost always abnormal, but definite hypsarrhythmia (a term coined by Gibbs and Gibbs in 1952 for a grossly abnormal encephalographic pattern marked by very high-voltage, random, slow waves and spikes in all cortical areas, giving the impression of a nearly total disorganization of cortical voltage regulation) was found in only 50% of the first records; the others showed an epileptic abnormality which was often severe. By contrast, more than 50% of the patients with epilepsy (not infantile spasms) in the same age-group have a normal electroencephalogram, and a hypsarrhythmic record is rare. Although a nonhypsarrhythmic, epileptic record may be found in patients with infantile spasms, electroencephalographic examination of suspected patients is useful, for a normal record is strongly against the diagnosis, while a hypsarrhythmic one is very much in favor of it.

Essential Hypertension in Childhood: A Clinical Contribution. B. Fantuzzi and N. Svilokos. Minerva pediat. 11:69-77 (Feb. 4) 1959 (In Italian) [Turin, Italy].

The authors discuss a case of benign essential hypertension in a 6-year-old girl with a family history of hypertension. Arterial hypertension, associated with sudden pallor, headache, and vertigo, developed a month after an adenotonsillectomy at the age of 4. The episodes, which subsequently included vomiting, were repeated once a week, and they soon took place daily. The maximum arterial blood pressure oscillated between 160 and 200 mm. Hg. Although there was no evidence of a lesion in the urinary tract, the patient had been treated for renal hypertension before admission. During a 54-day hospitalization she received Hydergine, a hypotensive compound consisting of dihydroergocornine, dihydroergocryptine, and dihydroergocristine. Hypertension persisted during and after hospitalization, with maximum basal values from 155 to 160 mm. Hg and minimum basal values from 95 to 115 mm. Hg. Laboratory findings excluded the presence of a renal lesion, pheochromocytoma, aortic coarctation or other cardiovascular malformations, and intracranial tumor.

In differentiating between benign and malignant arterial hypertension, the authors are more inclined toward the diagnosis of the benign form in this patient for the following reasons: 1. The arterial pressure never exceeded, except under emotional stress, the values of 160/115 mm. Hg. 2. A marked cardiac hypertrophy was absent on clinical, roentgenologic, and electrocardiographic examinations. 3. The level of azotemia persisted within the normal values. 4. There was no evidence of angiospastic retinitis. 5. Maximum arterial hypertension from 150 to 160 mm. Hg persisted for 6 years after discharge. 6. A slight daily headache was present, but there was no recurrence of vomiting and vertigo. 7. There was partial but durable response to the hypotensive medicament, which was administered for a short time.

The Family Physician and the Mentally Retarded Child. E. H. Watson. Postgrad. Med. 25:301-309 (March) 1959 [Minneapolis].

The family physician must summon all his skill as a counselor when he delivers a deformed or mentally defective child or is consulted about mental retardation. In the case of Mongolism or extreme microcephalia, it is rather evident from the beginning that the child's future, so far as mental development is concerned, can never be normal. However, so long as the presence of one of these abnormalities is only suspected, the best course is to put a carefully worded note on the infant's chart, with an outline of a definite plan to continue observations and to get consultation as needed to make a definite diagnosis, before acquainting the parents with the strong probability of mental defectiveness. It often requires all the art of the practice of medicine to avoid the appearance of inconclusiveness or evasiveness, on the one hand, and the unwarranted arousing of parental fears for the future development of their child, on the other hand. Failure of the infant to cry, suck, and feed normally shortly after birth may serve as a warning to the physician. The appearance of abnormal signs, such as cyanosis, twitching, or frank convulsive seizures, is ominous, but does not necessarily indicate that the central nervous system is abnormal or that it has been damaged beyond complete recovery.

Growth and development during the first few weeks and months proceed rapidly, and the experienced physician should be able to recognize signs of delay of development by the time the child is 3 or 4 months old. The monthly checkup should include observations and a notation on the chart of the child's approximate developmental stage. There is more than one reason for failure of mental growth and development to proceed in a normal fashion. In order that a correct and complete diagnosis may be made, the physician should keep in mind the various causes of mental deficiency (such as hereditary and prenatal causes, metabolic disorders, cranial maldevelopment, cerebral injury, and degenerative disorders) and of pseudomental deficiency, a term used to designate the condition of a child who is not behaving in a normal manner, due to sensory defects, cerebral palsy, chronic illness, emotional disturbance, psychosis, and environmental retardation, but who subsequently is not found to be mentally retarded. The author has found the experienced psychologist of the greatest aid in helping distinguish the mentally retarded child from the pseudomentally retarded one, and also to distinguish a child with a brain injury from the simple, genetically mentally inferior child. Often the services of an otologist or ophthalmologist may be needed in order that the child's hearing or sight may be accurately evaluated. There are state and national agencies on which the physician can call for help and advice to the parents of the deaf or blind preschool child.

It appears to be a conservative estimate that 60% or more of mentally defective children are so because of heredity. It is necessary to tell any parents of a defective child that the fact that they have produced a defective child, whether it be on the basis of genetics, isoimmunization, or unfavorable placental implantation, has statistically reduced their chances of producing normal children in the future. Answers to questions commonly asked by parents of mentally retarded children are reviewed.

Acute Leukemia in Childhood and Its Treatment. L. Tuuteri, M. Donner and R. Wegelius. Ann. paediat. Fenniae 5:39-45 (no. 1) 1959 (In English) [Helsinki].

The histories of 180 children with acute leukemia, ranging in age from birth to 15 years, who were treated at the Children's Hospital in Helsinki during 1950-1957, were reviewed in order to evaluate the results of specific therapy in leukemia. The patients were divided according to their treatment into 3 groups. The first group consisted of 100 children, most of whom were hospitalized during the earlier years of the study. These children were subjected to transfusions and other supportive therapy; antibiotics and sulfonamides were given to some patients, but none received specific drugs. The average duration of life in this group was 3.7 months. The second group of 33 children received chiefly folic acid antagonists, and steroids were given to only a few patients. The treatment in most patients was of short duration, and maintenance therapy was not consistently given. The average survival in this group was 4.7 months. The third group of 47 children, the majority of whom were treated during the last 2 years of this study, received a combined treatment with steroids and antimetabolites. The survival of this group was 6 months for 50% and more than 17 months for 10%. This study shows that the antileukemic drugs can prolong the survival time in the majority of children with leukemia. An important fact to be taken into consideration is that prolonging the life of an individual child may give him the opportunity to benefit from a new and perhaps more effective drug.

Periarteritis Nodosa: Report of Three Cases Successfully Treated by Cortisone and A. C. T. H. I. Z. Yonis. Ann. paediat. 192:65-80 (Feb.) 1959 (In English) [Basel, Switzerland].

The author cites previous reports indicating that periarteritis nodosa is recognized during life in a relatively small percentage of patients, and that the number of patients who recover either spontaneously or after treatment is limited. In recent reports on successful treatment, recovery was said to depend on whether the treatment had been started before vital organs were affected. This report is concerned with 3 children in whom periarteritis nodosa was diagnosed and successfully treated. There were 2 boys and 1 girl, ranging in age from 6 to 9 years. All had pain in the abdomen and in the lower extremities, cachexia, brownish-gray or bluish-gray color of the skin, profuse sweating, tachycardia, septic fever, leukocytosis, increased sedimentation rate, absence of reaction to antibiotics, appearance of nodules in the skin (in the first patient 66 days, in the second 16, and in the third 11 days after admission). Two patients had melena; one had characteristic roentgenologic findings in the ureters. The migrating pain, the septic fever, the nodules in the skin, and the roentgenologic findings in the ureters were of particular diagnostic importance. The diagnosis of periarteritis nodosa was corroborated in all 3 children by biopsy of subcutaneous nodules. Such nodules are transitory, and, as observed in the cases presented, they may disappear after a few days or even after a few hours. Therefore, one must look for them repeatedly. The biopsy of nodules offers the best chance of a positive histological diagnosis. In patients in whom periarteritis nodosa is suspected, histological examination should be repeated several times before a negative biopsy report is accepted as definite.

Steroid treatment should be started in every case suspected of periarteritis nodosa even before the clinical diagnosis is confirmed by histological examination. The influence of treatment with cortisone or corticotropin (ACTH) is manifested by a fall in the temperature within the first 24 to 36 hours. If no immediate change occurs, another steroid or ACTH should be given. Fall in temperature, improvement in the patient's general condition, and a more active attitude serve as indications of a favorable reaction to steroids. The sedimentation rate does not reflect the clinical course. The dosage of cortisone or ACTH must be individualized; treatment must be given up to the tolerance limit of the patient and continued without interruption until its discontinuance is not followed by exacerbation. Of the patients presented, one responded to treatment with cortisone. The condition of the second patient deteriorated during the administration of cortisone but improved after treatment with ACTH. The third patient improved after receiving ACTH only.

Absence of Intestinal Viral Flora in Infants During Epidemic of Escherichia coli Gastroenteritis. V. M. Young, J. Warren and R. B. Lindberg. Proc. Soc. Exper. Biol. & Med. 100:579-581 (March) 1959 [Utica, N. Y.].

The authors point out that many instances have been recorded in which specific strains of Escherichia coli have been isolated from most, or all, cases in outbreaks of infant diarrhea. Several investigators suggested the possibility that such diarrheas are the result of interaction between the pathogenic bacterium and a virus. The studies described in this paper investigated this possibility. Numerous Esch. coli 0-111:B_4 organisms were present in fecal samples obtained from all but 2 of 25 patients and were also isolated from one specimen of vomitus in an outbreak of diarrhea in infants. No Salmonella or Shigella organisms or pathogenic protozoa were found. Treated stool samples collected from 25 infants were inoculated into monkey-kidney and HeLa-cell tissue cultures, embryonated eggs, and a variety of young animals by various routes. No viral agent could be detected. It is concluded that this outbreak of gastroenteritis was caused by Esch. coli 0-111:B_4, uncomplicated by other microbial agents.

Exchange Transfusions by Catheterization of the Abdominal Aorta in Newborn Infants. E. Saling. Geburtsh. u. Frauenh. 19:230-235 (March) 1959 (In German) [Stuttgart, Germany].

The author performed successfully 3 exchange transfusions in newborn infants by introducing immediately after birth 2 catheters into the abdominal aorta of the infants. With the umbilical cord still pulsating, one catheter was introduced through an incision about 3 cm. above the umbilical ring into one of the umbilical arteries, and a second catheter was introduced into the other umbilical artery; both catheters were passed by way of the corresponding internal iliac and common iliac arteries into the abdominal aorta. Passing of the catheter through the pelvic loop in the vascular track at the transition of the umbilical cord from the anterior abdominal wall to the small pelvis was carried out without difficulty, since a flexible plastic tube of polyvinyl chloride (1.5 mm. in diameter) was used. The catheter entering the aorta distal from the heart was used for the drip infusion of the donor blood, and the catheter entering the aorta proximal to the heart was used for the withdrawal of the infant's blood. This resulted in a highly improved technique of blood exchange. The injection of the donor blood and the simultaneous withdrawal of the infant's blood were accomplished in the simplest manner. The procedure is sparing and without danger for the infant.

For infants in whom one succeeds in introducing only one catheter into the abdominal aorta or in whom the second catheter becomes obstructed, the author recommends a modified technique in which one umbilical artery and the umbilical vein are used for catheterization; the donor blood should be injected by way of the artery, and the infant's blood withdrawn with the aid of the venous catheter which has a larger diameter (2.1 mm.). Three additional exchange transfusions were performed by this technique in infants with good results. For infants in whom erythroblastosis may be recognized only after birth, an improved exchange transfusion technique is recommended in which 2 catheters are introduced into the umbilical vein.

The blood oxygen saturation was studied in the course of the exchange transfusions. The degree of oxygen saturation was gradually reduced by 20% after the institution of the transfusion in several of the infants, and that despite well-functioning respiration and satisfactory cardiac performance. The saturation values increased rapidly when oxygen was administered by means of a tracheal tube. Routine administration of oxygen seems, therefore, to be justified in the course of every exchange transfusion in infants.

Effects of Season and Temperature on Childhood Plumbism. A. M. Baetjer. Indust. Med. 28:137-143 (March) 1959 [Chicago].

A review of the literature on lead poisoning in children revealed a marked seasonal distribution with almost all the cases occuring between the months of May and October. This seasonal distribution has been attributed to various factors, such as exposure to the ultraviolet radiation from the sun in summer and the resulting increase in vitamin D which increases the absorption of lead from the intestines and the deposition of lead in the bones. The increase in environmental temperature during the summer months also has been suggested as a factor responsible for the seasonal distribution of acute lead poisoning cases in children.

A series of experiments was carried out in the laboratory of Johns Hopkins University in Baltimore to study the effects of environmental temperature and humidity on the susceptibility of mice to lead poisoning. The animals were injected either intraperitoneally or intravenously with a single dose of lead acetate or lead nitrate sufficient to cause death in about 20 to 40% of the mice at a temperature of 72 F with about 50% relative humidity. Exposure to a high temperature of 95 F increased the mortality significantly, hastened the onset of deaths and accelerated the rate of dying. Because children sweat in high temperatures and may become dehydrated, it seemed possible that the seasonal distribution of lead poisoning in children might be attributed to dehydration rather than to the high temperature. Dehydration was produced in mice by restricting water intake. Dehydration significantly increased the mortality at temperatures of 72 and 95 F and hastened the onset of deaths at the high temperature.

In additional experiments the effect of high temperature on chronic lead poisoning was studied in mice. In these experiments the mice were injected intraperitoneally 6 days per week with smaller doses of lead nitrate than those used in the acute experiments. The mortality was significantly higher and the latent time significantly shorter in the lead-injected mice exposed to a temperature of 95 F than in those kept continuously at a temperature of 72 F. The physical mechanism responsible for the higher mortality and the more rapid onset of illness and death in the animals at the higher temperature is not clear. The excretion of lead in the urine and feces of the mice was compared at 72 F and 95 F temperatures. The determinations showed that at the higher temperature the animals excreted significantly less lead in their urine over a period of 14 days after the intravenous injections of lead than did the animals kept at 72 F. The total fecal output of lead was also somewhat less at the high temperature.

Ataxia Teleangiectatica. C. E. van der Hoog. Maandschr. kindergeneesk. 27:26-33 (Jan.) 1959 (In Dutch) [Leiden, Netherlands].

The author calls attention to a report by Boder and Sedgwick (abstracted, J. A. M. A. **167**:1435 [July 12] 1958), which cited 8 children with progressive cerebellar ataxia, all of whom had telangiectasia of the bulbar conjunctiva and a butterfly-shaped area of the face. The patients also were subject to recurrent respiratory infection, which gave rise to bronchiectasis. Van der Hoog presents the case of a 15-year-old girl who had progessive cerebellar ataxia and typical telangiectasia of the bulbar conjunctiva. The patient was hospitalized 7 times for recurrent pulmonary infections. When she was 7 years old, lobectomy and lingulectomy of the left lung had been performed on account of extensive bronchiectasis, but there was no improvement; respiratory infections continued to occur. Neurological examination revealed grimacing, athetotic movements of arms and legs, a peculiar speech defect, convergent strabismus, and an ataxic walk.

The syndrome presented by this patient had a striking resemblance to that described by Boder and Sedgwick under the term "ataxia telangiectasia." The author feels that "familial" could be added to this term, since the syndrome has at times been observed in several members of a family. The recurrent infections of the respiratory tract should be treated in order to avoid bronchiectasis. These infections are about the only aspects of the syndrome that can be treated; the ataxia is progressive and eventually leads to complete invalidism. Children with this syndrome have average intelligence, although their facial expression may suggest mental deficiency.

DERMATOLOGY

The Treatment of Dermatomycoses with Orally Administered Griseofulvin. H. Blank and F. J. Roth Jr. A. M. A. Arch. Dermat. **79**:259-266 (March) 1959 [Chicago].

Griseofulvin, a colorless, neutral, thermostable antibiotic isolated from Penicillium griseofulvum, was used in treating 22 male and 9 female patients, between the ages of 5 and 71 years, with mycoses caused by various species of dermatophytes. Eighteen of the 31 patients received orally 1 Gm. of the antibiotic daily, while the other patients were given daily doses varying from 1.5 to 5 Gm. The duration of treatment varied from 10 days to 15 weeks. The organisms causing the mycoses included Trichophyton rubrum (27 patients), Candida albicans, T. mentagrophytes, T. tonsurans, Microsporum audouini, M. canis, Malassezia furfur, Epidermophyton floccosum, and Blastomyces dermatitidis.

The patients showed a uniformly favorable response to oral therapy with griseofulvin. Those with infections of long duration, up to 60 years, seemed to respond as readily as those with infections present for a few weeks or months. Infections caused by C. albicans, M. furfur, and B. dermatitidis did not seem to respond to this therapy. Tinea corporis usually cleared in 1 or 2 weeks; itching usually ceased in 3 to 5 days. Tinea pedis improved within 1 or 2 weeks but sometimes required 3 or 4 weeks or longer to clear. Tinea capitis improved within 2 or 3 weeks but occasionally required more prolonged treatment. Onychomycosis required 3 or 4 months to clear, but new normal nail growth was seen earlier. Cultures of epithelial lesions often became negative in one week. Direct potassium hydroxide preparations became negative in about 2 weeks. Infected hair and nails appeared to contain viable fungi until the involved portions were replaced by healthy new growth.

Although toxic reactions appear to be minimal with therapeutic doses in man, animal experiments indicate that repeated peripheral blood cell counts at least should be performed during a course of prolonged therapy. An urticaria-like drug eruption occurred after 6 weeks of continuous therapy in one patient, and others had mild self-limited complaints of gastrointestinal distress and headache. A daily dose of 1 Gm. of the antibiotic seems to be adequate, although the minimum effective dose and the optimum dose have not been established for all types of infection. The duration of treatment required probably will vary, apparently depending on the time required for normal replacement of the infected tissues. Likelihood of relapse or recurrence of infection is as yet not known.

Some Practical Aspects of the Diagnosis and Management of Shoe Dermatitis. A. A. Fisher. A. M. A. Arch. Dermat. 79:267-274 (March) 1959 [Chicago].

The diagnosis of shoe dermatitis depends on the history, the clinical picture, positive patch-test reactions to shoe material, and the patient's ability to wear proper substitute shoes without dermatitis. In the author's patients with shoe dermatitis, rubber —either in the rubber thermoplastic box toe or in the rubber cements—was the commonest cause of allergic contact dermatitis. This rubber sensitivity was apparently most often due to additives, such as antioxidants and accelerators. Chromates, dyes, and nickel also occasionally caused allergic contact shoe dermatitis.

The materials used by the author for a "screening" patch-testing shoe tray included thermoplastic rubber box-toe material, 1% monobenzyl ether of hydroquinone in petrolatum, 1% 2-mercaptobenzothiazole in petrolatum, 1% tetramethylthiuram monosulfide in petrolatum, 0.25% aqueous potassium dichromate, 2% paraphenylenediamine in petrolatum, and 5% aqueous nickel sulfate solution. Details are given as to how to obtain these materials and how to prepare them for patch testing. Use of such a shoe tray may facilitate the diagnosis of allergic contact dermatitis and obviate the necessity for the dissection of shoes to obtain materials for patch testing. However, negative reactions to the substances in the patch-testing tray do not necessarily exclude shoe dermatitis. It may be necessary to test with materials from the suspected shoe. The names and addresses of shoe manufacturers and retailers are given from whom shoes may be obtained which are free from certain known specific sensitizers.

Nonspecific factors also may play their part in shoe dermatitis. Perspiration can leach out chromates, rubber additives, and dyes from shoes and thus cause contact of these potential sensitizers with the skin. Ill-fitting shoes and certain foot abnormalities may cause excessive friction and wearing away of protective inner shoe linings and allow more intimate contact of shoe sensitizers with the skin. The use of a noncaking dusting powder (fluffy tannic acid, boric acid, bentonite, and purified talc dispensed in a sifter box) may occasionally prevent dermatitis by reducing perspiration. Also, orthopedic correction of various deformities or the wearing of special orthopedic shoes may be necessary to correct certain types of shoe dermatitis not necessarily of the allergic contact type.

A Contrast of Cutaneous Cancer as Observed in Texas and in Minnesota. F. W. Lynch, C. F. Lehmann and J. L. Pipkin. A. M. A. Arch. Dermat. 79:275-283 (March) 1959 [Chicago].

Comparison of 2 series of patients with cutaneous cancer from 2 practices in the northernmost (Minnesota) and southernmost (Texas) areas of the United States, in which there is great difference in temperature and total hours of clear sunlight, revealed that cancer of the skin is much more frequently observed in Texas than in Minnesota. Both the basal-cell lesions and the squamous-cell lesions occurred at earlier ages in Texans than in Minnesotans. Basal-cell lesions occurred more frequently in women. They occurred at earlier ages than did squamous-cell lesions other than those of the neck and the lower lip, which were seen almost exclusively in men and more frequently in Texans. Actinic exposures appear to explain these differences, but they do not explain completely the behavior of basal-cell epitheliomas. If basal-cell epitheliomas relate with actinic exposure, then why do they occur earlier in women than in men? Greater actinic exposure is not likely to be great enough for the complete explanation. However, difference in actinic exposure may be at least part of the explanation for greater absolute, not relative, incidence of basal-cell epitheliomas among Texans, the occurrence in that state at an earlier age, and the relatively greater incidence of such lesions on the forehead, as compared with patients in Minnesota.

Behavior of Glutamic Pyruvic Transaminase in Blood Serum and in the Serum of Blisters in Patients with Eczema and Bullous Dermatoses. G. Weber and H. Theisen. Arch. klin. u. exper. Dermat. 208:93-97 (no. 2) 1959 (In German) [Berlin].

The investigation of the behavior of glutamic pyruvic transaminase (GP-T) in patients with skin diseases seemed important after it had been demonstrated that another aminopherase, glutamic oxalacetic transaminase (GO-T), exhibited a much greater activity in the intraepidermal space of the cantharides blister and of the spontaneous blister than in the blood serum of the same patient. The authors compared the GP-T activity in the serums of blood and of skin blisters in 20 patients with skin lesions of the eczema-dermatitis group (weeping eczema, eczema rhagadiforme, intertriginous eczema, lichenoid eczema, dermatitis, and diffuse neurodermatitis), and in 9 patients with bullous dermatoses (erythema exudativum multiforme, pemphigus vulgaris, bullous serum exanthem, bullous photodermatoses, and dyshidrosis). In preliminary studies on persons without skin or metabolic disorders, the authors had found that the activity of GP-T in 1 ml. of blood serum was in the range of 5 to 35 units. These values corresponded to those obtained by Wroblewski of New York.

The values obtained in the 2 groups of patients are tabulated. In the patients with lesions of the eczema-dermatitis group, the activity of the GP-T was within the normal range in the blood serum as well as in the blister fluid. The only exception was a diabetic patient with intertriginous eczema, in whom the activity was much higher in the blisters than in the blood serum. The values in the blisters and in the blood serum in the individual patients showed no great differences, and the differences that existed showed no regularity or any relationship to the existing skin lesion. The same lack of relationship between GP-T activity and skin process was evident in the group of patients with bullous dermatoses. Thus, the results of these studies speak against, rather than for, the development of this aminopherase in the human skin.

The Hypereosinophilic Syndrome with Specific Cutaneous Changes (Eosinophilic Leukemoid). L. Pfleger and J. Tappeiner. Arch. klin. u. exper. Dermat. 208:98-115 (no. 2) 1959 (In German) [Berlin].

Cutaneous eosinophilic granulomas have been observed in many dermatoses. Eosinophilia of the tissues, "histoeosinophilia," is widely regarded as the manifestation of an allergic phenomenon, but it is still a question whether the histoeosinophilia of disorders designated by some investigators as "symptomatic eosinophilia" and by others as "cutaneous eosinophilic pseudogranulomas" is likewise an allergic reaction elicited by local tissue breakdown. The allergic origin of the eosinophilia of the blood and bone marrow has been experimentally demonstrated. It is generally accepted as a manifestation of a hypersensitivity reaction in serum disease, anaphylaxis, bronchial asthma, allergic rhinitis, allergic enteritis, angioneurotic edema, urticaria, purpura, helminthiasis, drug intoxications, and so on. Even the so-called familial eosinophilias are related to allergic diseases. Symptomatic eosinophilias differ from another group of allergic diseases, in which the blood picture is leukemoid.

The authors describe the symptom complex of eosinophilic leukemoid on the basis of the history of a woman (born in 1913), in whom an eosinophilia ranging from 13 to 70% had been demonstrated repeatedly between 1948 and 1958. The leukocyte count ranged at times up to 23,000 per cubic millimeter, and this was accompanied by generalized swelling of the lymph nodes and peculiar cutaneous lesions. The skin lesions began when the patient was 24 years old, and took the form of itching papular eruptions on the extremities, which became intensified by exposure to dusts (threshing) and by certain foods. At the age of 39 (in 1952) the woman for the first time showed erythematous swelling of the orbital, palpebral, and perioral regions with inflammatory infiltration at the angle of the mouth and with generalization of the papular exanthem. Various diagnoses were considered. The severe and persisting blood eosinophilia in the presence of leukocytosis and skin lesions even suggested a myeloid, eosinophilic leukemia, but this was rejected because of the long duration of the disease and on the basis of the myelogram.

Eosinophilic leukemoid was considered because the woman had the following signs characteristic of this disorder: persisting eosinophilia in the presence of leukocytosis; generalized swelling of lymph nodes; enlargement of liver and spleen; long duration of the disease with survival; and histological findings in lymph nodes and liver. The cutaneous changes had not been described in earlier reports on this syndrome. The histological aspects of the skin lesions, however, particularly the inflammatory reticulogranulomatous proliferation and the excessive number of eosinophils, corresponded to the allergic-hyperergic reaction of the tissues. In this woman not only the shock organs of first rank (bone marrow, blood, and liver) but also those of second rank (skin) were involved.

Various factors, such as helminths, bacteria, pollen, and foods, may play a part in the etiology of eosinophilic leukemoid, which is known also as the hypereosinophilia syndrome, but its pathogenesis is uniform in that it represents an allergic reaction in an hyperergic organism which, as a result of constitutional factors, is predisposed to hypereosinophilia. The lack of the histaminopexic capacity of the serum, demonstrated by Parrot's histaminopexic test, provided additional proof of the existence of an allergic reaction in a sensitized organism.

UROLOGY

Mortality Following Prostatectomy. P. G. Fox, Jr. and A. I. Dodson, Sr. North Carolina M. J. 20:67-69 (Feb.) 1959 [Winston-Salem].

A total of 362 prostatectomies were performed at the Medical College of Virginia in Richmond during the years from 1941 through 1946 (1945 excluded). Of those procedures, 291 were transurethral resections, while 71 were open procedures through either the suprapubic or the perineal approach. Thirteen deaths followed the transurethral resections, while 7 deaths followed the open procedures. From 1952 through 1956, 983 prostatectomies were performed, of which 798 were transurethral resections and 185 were open procedures by the suprapubic, retropubic, and perineal approaches. Seven deaths followed the transurethral resections, while 6 deaths followed open operations. The mortality following transurethral resections in the earlier period was 4.4%, with a decrease to 0.87% in the later period. There was also a similar drop in mortality after open prostatectomy from 9.9 to 3.2%, making an over-all decrease from 5.5 to 1.3%.

Comparing these figures with those reported in the literature, the authors found that there were 160 deaths among 7,910 patients undergoing transurethral resections during 1940-1945. Mortality varied among reports from 0.8 to 14%. One thousand two open-prostatectomy procedures, with 67 deaths, were reported during the same years. Mortality again varied greatly among reporting authors, ranging from 1 to 16.7%. During the years from 1950 through 1955, 5,715 transurethral resections were reported, with 81 deaths; and 2,123 open-prostatectomy procedures, with 38 deaths. The average mortality following transurethral resection was 2.1% in the earlier period, with a decrease to 1.4% in the later period. A similar drop in mortality was noted following open prostatectomy, from 6.7 to 1.8%. The authors feel that the slight difference in mortality after transurethral resection and after open prostatectomy during the recent period is probably due to the fact that more transurethral resections are carried out on poor-risk patients.

The over-all decrease in mortality from prostatectomy has been from 2.6 to 1.5%. An analysis of the causes of death after prostatectomy revealed that cardiopulmonary complications ranked first in both periods. It is suggested that electrocardiographic studies be added to the other routine examinations in evaluating the patient preparatory to prostatectomy. This will at least make it possible to identify the patients most likely to have cardiovascular complications and to plan the treatment accordingly. Only by careful preoperative evaluation and postoperative care will it be possible to reduce the mortality from prostatectomy in the future.

Combination of a New Synthetic Estrogen with Cytostatic Action and Prednisone in the Treatment of Prostatic Cancer. A. Toffol and L. Cattani. Arch. ital. urol. 31:439-458 (Jan. 20) 1959 (In Italian) [Bologna, Italy].

Seven patients with prostatic cancer received one or more courses of an Italian preparation of hexestrol diphosphate (Citostasina) combined with prednisone and supplemented by the administration of corticotropin (ACTH). A course of treatment consisted of a daily dose of 500 mg. of Citostasina administered intravenously twice a day for a week; half of this dose was subsequently administered for from 2 to 5 weeks. Prednisone was given orally in gradually diminishing daily doses, consisting of 15 mg. for each of the first 3 days, of 10 mg. for each of the succeeding 20 days, and of 5 mg. a day for the remaining period. ACTH was administered in doses of 10 units once every 5 days during this treatment.

This chemotherapeutic treatment proved to have an effective, but limited, cytostatic action. It was well tolerated, it produced almost no side-effects, and it had no feminization effects. The general state of health improved in all patients, pain decreased or disappeared, and the disturbances of urination, where present, subsided. The extent of the tumors and of metastatic lesions remained unchanged on roentgenologic or rectal examination. The authors believe that this combined chemotherapeutic management in patients with prostatic cancer, but without metastatic lesions, can complement the surgical therapy. It still seems to be the best choice even in those instances in which metastases are present, because it provides pharmacological adrenalectomy and orchiectomy by sole medical means.

OPHTHALMOLOGY

On Non-Penetrating Corneal Transplantation. G. de Ocampo and R. B. Espiritu. J. Philippine M. A. 35:1-10 (Jan.) 1959 [Manila].

Although many penetrating keratoplasties have been performed in the Philippines during the last 9 years, nonpenetrating or lamellar keratoplasty has been done rarely. In fact, lamellar keratoplasty is the least known of the developments in corneal transplantation. Central penetrating keratoplasty is not the ideal method for many of the Philippine patients requiring keratoplasty because of the extent, nature, and position of the leukoma or the vascularization, unevenness, thinning, or thickening of some areas. Some opacities do not involve the posterior layers of the cornea, and in these cases, if the vision is 20/100, 20/200, or slightly poorer, the risk of penetrating keratoplasty worsening the preoperative vision is disturbing to the surgeon, especially so if the other eye is completely blind. In these instances nonpenetrating is preferable to perforating keratoplasty.

Although many corneal surgeons consider nonpenetrating lamellar keratoplasty technically more difficult, the authors found that the corneal dissector recently designed by one of them (de Ocampo) greatly lessened the technical difficulties of lamellar keratoplasty and keratectomy. The de Ocampo dissector is designed to split stromal lamellae at their cleavage planes and also to cut the many minute interconnections between lamellae of different layers. With this dissector it is sufficient to cut only about one-fourth or less of the circumference of the cornea to dissect the whole corneal lamella up to and even beyond the limbus. The authors report observations on a series of 49 patients, whom they recently subjected to lamellar keratoplasties with the aid of the new corneal dissector at the Philippine General Hospital and at the de Ocampo Eye Hospital, in Manila. The series included patients with superficial corneal opacities, ocular pemphigus, extensive or recurrent pterygium, extensive leukomas, corneal ulcer, and corneal burn. Mechanical and biological problems of lamellar corneal grafting are discussed. Different methods are briefly reviewed, and the new technique is described. Representative cases are shown in illustrations. While the problems of infection, inflammation, and clouding, also viability of the donor cornea and diseases of the host, are the same with nonpenetrating as with penetrating keratoplasty, the nonpenetrating method, nevertheless, has several advantages. Since the endothelium and Descemet's membrane of the host are not replaced, the graft has better chances of nourishment, is less liable to be complicated by glaucoma and vascularization, and involves practically no danger of new anterior synechiae. The authors emphasize the expanding usefulness of lamellar keratoplasty.

Exophthalmos of Exophthalmic Goiter: ACTH and Cortisone Treatment. P. de Paula e Silva and W. da Silva Prado. Rev. paulista med. 54:101-106 (Feb.) 1959 (In Portuguese) [São Paulo, Brazil].

Two men, 54 and 30 years old, were hospitalized for treatment of exophthalmos of toxic goiter, which had lasted for 2½ years. The patients lost weight (20 and 12 kg. [44 and 27 lb.], respectively) during the last few months. The goiter was small and diffuse. Exophthalmos was marked, and the symptoms of hyperthyroidism were severe. The patients complained of extreme fatigability, various ocular symptoms of exophthalmos, pain in the eyes, and visual disorders. The treatment consisted of corticotropin (ACTH) and cortisone. ACTH was given intravenously in daily dosage of 40 units for 32 days to one patient and 35 days to the other. Cortisone was given by mouth in daily dosage of 200 mg. for 32 and 105 days respectively. The hormonal treatment caused a marked lowering of hyperthyroidism, diminution of the size of the goiter, disappearance of ocular symptoms and of ocular pain, and improvement of vision. The satisfactory results remained unchanged for 3 months, when a subtotal thyroidectomy was performed. The first patient was discharged after the operation in satisfactory condition with good immediate and late results. In the second patient the immediate results of subtotal thyroidectomy were excellent. However, on the 4th day after the operation the patient exhibited an attack of psychosis with mental depression, hemiparalysis on the right, and coma. He did not react to prednisone administered orally and to the intravenous administration of dextrose and died on the 6th day after the operation. Apparently the attack was due to the prolonged administration of cortisone. Autopsy revealed only moderate edema of the left cerebral hemisphere.

According to the authors, exophthalmos of toxic goiter is due to hypersecretion of thyrotropic hormones, which results from an imbalance of thyrotropic and corticosuprarenal hormones at the level of the thalamus-hypophysial system. ACTH and cortisone normalize the hormonal imbalance and also the secretion of thyrotropic hormone and prepare the patients, for a certain time, for a favorable general and metabolic state for a subtotal thyroidectomy followed by good results.

Incontinentia Pigmenti Associated with Changes in the Posterior Chamber of the Eye. J. G. Cole and H. G. Cole. Am. J. Ophth. 47:321-328 (March) 1959 [Chicago].

The authors were consulted about a 4½-month-old boy because of bilateral ocular abnormalities which on examination proved to involve a mass in the posterior chamber. Because of a striking skin condition, a dermatologist was consulted, and on the basis of clinical examination and histological study, a diagnosis of incontinentia pigmenti was made. Because the growth in the left eye strongly suggested glioma, the eye was enucleated. The greater part of the iris angle was obliterated by adhesion of the iris over most of the limbus, but the marginal sinus was clearly identified and included cysts in some areas. The iris was atrophied and distorted, and the pigment lay several millimeters over the posterior surface. On one side a newly formed membrane extended from the iris to the cornea. The ciliary body and ciliary processes were deformed by traction on the posterior surface of the lens. A membrane had formed on the ciliary body due to chronic cellular exudate and fibrin deposition. The choroid and sclera were not altered except in the area near the nerve where there was considerable inflammatory reaction extending through the cribriform plate into the vaginal sheath. The retina was completely detached and incorporated into a membrane that extended across the retrolental space and also extended posteriorly to the optic nerve, which it tended to pull forward. The normal cellular structure of the retina was hidden in the massive fibrous detachment by a cyst which separated its layers on one side. Both the cyst and the space back of the retina were filled with clear, pink-staining fluid containing some debris.

Seven cases of typical incontinentia pigmenti were collected from the literature, in all of which the diagnosis was confirmed by histological study of the skin lesion. The findings in these 8 patients showed that the syndrome of incontinentia pigmenti usually includes associated congenital defects besides those of the skin. In about one-third of the cases the dysplasia is manifested in one eye, sometimes in both eyes, but rarely to the same degree in both eyes. The mass in the posterior chamber associated with incontinentia pigmenti seems difficult to distinguish from retrolental fibroplasia. It is, however, a congenital lesion, occurs usually in infants born at term, and is most frequently unilateral. The masses in the posterior chamber of the eye in patients with incontinentia pigmenti are clinically more variable than those of retrolental fibroplasia and are also more likely to be associated with other congenital defects of the eye. The more severe cases of mass in the posterior chamber can usually be differentiated from neoplasm by the presence of other congenital anomalies or defects in metabolism, and occasionally by the presence of similar defects in the family, suggesting a genetic factor. As far as is known, provisional diagnosis of neoplasm has not been established in any of these cases.

Ocular Sarcoidosis. D. G. James. Am. J. Med. 26:331-339 (March) 1959 [New York].

Ophthalmic involvement was observed in 50 (25%) of 200 patients with clinical or radiologic features of sarcoidosis supported by histological evidence of sarcoid tissue. The ocular manifestations included those of subacute iridocyclitis in 11 patients or chronic iridocyclitis in 19 patients, phlyctenular or nonspecific conjunctivitis in 8 patients, keratoconjunctivitis sicca in 7 patients, follicular collections in the conjunctival fold of the lower eyelid in 3 patients, retinal periphlebitis in 1, and cataracts in 1. Patients with subacute iridocyclitis had a sudden onset, clinical evidence of inflammation, and occasional complete clearing within 6 months, whereas chronic iridocyclitis developed insidiously and persisted because of complicating ocular fibrosis. Subacute iridocyclitis was accompanied by transient skin lesions in contrast to chronic iridocyclitis which was accompanied by indolent skin lesions. These striking differences may have been in part due to corticosteroid therapy which was practiced within days, or at most weeks, of the onset of symptoms in most of the patients with subacute iridocyclitis, whereas patients with chronic iridocyclitis had waited several years for the introduction of corticosteroid therapy which has probably changed the natural history of sarcoid iridocyclitis. Ocular sarcoidosis was commonly accompanied by intrathoracic and cutaneous lesions of sarcoidosis and by lymphadenopathy. Reduced secretions due to simultaneous involvement of lacrimal and parotid glands superficially resembled Sjögren's syndrome in 2 patients.

Comparison of the 50 patients who had ocular lesions with the 150 patients who did not have ophthalmic involvement revealed that the patients with ocular sarcoidosis belonged to an older age group in which the peak occurred in the 4th or 5th decade with a mean age at onset of 39 years; women predominated, and the patients' reactions to Mantoux tests were more often negative. Histological evidence of sarcoid tissue was obtained by biopsy of various tissues and also by means of Kveim's skin test which gave positive results in most of the patients with ocular sarcoidosis. Blind conjunctival biopsy was of no diagnostic help. The natural course of sarcoidosis is toward spontaneous healing by fibrosis. In the eye this may cause serious complications, and, therefore, ocular involvement is an absolute indication for early and energetic corticosteroid therapy.

THERAPEUTICS

Anticoagulant Therapy: Clinical Experience With Acenocoumarin (Sintrom) and Other Coumarin Derivatives. Y. Desrochers, N. Aérichidé and P. David. Am. Heart. J. 57:321-326 (March) 1959 [St. Louis].

Anticoagulant therapy with coumarin derivatives has been employed in 382 patients, 305 of whom received acenocoumarol (Sintrom), 40 received bishydroxycoumarin (Dicumarol), and 37 received ethyl biscoumacetate (Tromexan). Experience with these anticoagulants during 4 years of study has included a total of 650 patient-months of therapy, of which 604 patient-months represent treatment with acenocoumarol. Of the 382 patients, 287 demonstrated coronary artery disease, and 95 presented other cardiovascular diseases. The Quick prothrombin time test was used in all cases to measure the adequacy of therapeutic control.

Of the 3 coumarin derivatives studied, acenocoumarol proved to be far more potent than either bishydroxycoumarin or ethyl biscoumacetate for anticoagulant therapy, particularly in patients with coronary artery disease who require maintenance for long periods of time. The optimum loading dose of acenocoumarol employed in the 305 patients was 11 to 25 mg. over a period of 18 to 60 hours. The condition of the patients was thereafter maintained satisfactorily on an average dose of 3.6 mg. daily. It has been observed that a much lower dose of acenocoumarol is required for induction when the prothrombin time is prolonged to begin with. Induction can be accomplished most satisfactorily in such patients with half the usual loading dose. Patients with renal or cardiac insufficiency also require smaller doses of acenocoumarol. Induction of therapy in 43 of the 305 patients with right heart failure was accomplished, on the average, with 16 mg. of acenocoumarol over 48 hours; the maintenance dose thereafter was 3.1 mg. Patients with uremia required no reduction of the loading dose, but their condition was maintained satisfactorily on doses averaging 2.7 mg. The therapeutic levels of hypoprothrombinemia in the 40 patients receiving bishydroxycoumarin could be established after 3 to 6 days with a loading dose averaging 445 mg. during the first 48 hours, followed by a maintenance dose averaging 79 mg. daily. Equivalent results were obtained in the 37 patients receiving ethyl biscoumacetate with a loading dose of 1,280 mg. during the first 24 hours and a daily maintenance dose averaging 387 mg.

While the effect of bishydroxycoumarin is sufficiently stable to be useful, its delayed action necessitates that heparin be used initially, and the persistence of hypoprothrombinemia after withdrawal increases the danger of hemorrhagic complications. Ethyl biscoumacetate, whose action is rapid and more easily subject to control, has produced in a number of patients marked fluctuations in prothrombin levels. The action of acenocoumarol, on the other hand, is intermediate in onset and duration, and prothrombin time is easily maintained within a therapeutic range. Hemorrhagic and thromboembolic accidents were infrequent in the patients of this series, and it appears that the mortality of patients with coronary artery disease is markedly reduced by anticoagulant therapy.

Restoration of Sinus Rhythm in Experimental and Clinical Ventricular Arrhythmias by Methoxamine Hydrochloride. I. C. Brill, J. D. Krueger and E. L. McCawley. Am. J. Cardiol. 3:307-313 (March) 1959 [New York].

Methoxamine (Vasoxyl) hydrochloride was given to dogs in which ventricular arrhythmias had been produced by various experimental procedures; these included the ligation of the left anterior descending coronary artery; the production of myocardial necrosis by injecting, through the intact chest, a suspension of zinc hydroxide into the left ventricular wall; and the intravenous administration of an overdose of digoxin and acetyl strophanthidin. Bigeminal rhythms were produced in the dogs by a new experimental procedure consisting of continuous intravenous infusion of amodiaquin (Camoquin) hydrochloride. Methoxamine administered in doses of 0.5 to 1 mg. per kilogram of body weight suppressed the various ventricular arrhythmias in the dogs for periods of 30 to 60 minutes.

Methoxamine then was given a therapeutic trial in 14 hospitalized patients with ventricular arrhythmias. The drug was administered intravenously by diluting the contents of an ampul, 20 mg., in 250 cc. of 5% dextrose. In a few instances the drug was given by intermittent intramuscular injection. Of the 14 patients, 11 had ventricular arrhythmias associated with myocardial infarcts; 1 with diffuse coronary sclerosis had ventricular arrhythmia believed to be the result of digitalis intoxication; and 2 had ventricular arrhythmias, either irregular or coupled, occurring without any apparent cause. The maximum dose of methoxamine given to the 11 patients was 20 mg. administered over a period of 20 minutes. The patient with digitalis intoxication was given a total dose of 10 mg. Of the 2 patients with arrhythmia of unknown causation, one with multifocal ventricular arrhythmia received a total dose of 5 mg. of the drug, and the other with persistent quadrigeminal rhythm received a total dose of 25 mg. As in the experimental animals, methoxamine in single doses was capable of suppressing clinical ventricular arrhythmias in most of the patients for periods of 20 to 40 minutes. After myocardial infarction the drug was as effective in patients with normal blood pressure as in those with hypotension or in shock.

The Insulin Equivalence of Salicylate. J. Reid and T. D. Lightbody. Brit. M. J. 1:897-900 (April 4) 1959 [London].

The authors studied the insulin equivalence of aspirin in 9 women and 5 men, between the ages of 33 and 74 years, with diabetes mellitus, whose insulin requirements as outpatients ranged from 14 to 112 units per day. The amount of insulin which could be replaced by a maximal tolerated course of aspirin was determined in each patient. Aspirin therapy was started and insulin therapy continued. Aspirin was administered in doses varying between 0.7 and 1.5 Gm. given 5 times daily to attain maximum therapeutic serum salicylate levels of 35 to 45 mg. per 100 cc. and to give the drug every opportunity to exert a full therapeutic effect under well-controlled conditions. Estimations of the fasting blood sugar level and urinary sugar were continued, and insulin administration was reduced progressively if warranted by the biochemical findings. Nine patients whose condition was well controlled with insulin had good responses to aspirin. The largest quantity of insulin zinc suspension replaced completely with aspirin was 48 units; the largest reduction in insulin requirement was 72 units in the patient receiving 112 units daily. The condition of 5 patients, which was poorly controlled with insulin, was not materially improved with aspirin therapy. It was concluded that aspirin was most effective in patients who responded well to insulin, and vice versa. The findings in patients whose condition was well stabilized with insulin also suggested that, the higher the insulin requirement, the greater was the amount of hormone that might be replaced by aspirin.

Transient but serious symptoms of anorexia and nausea developed in 7 patients and went on to vomiting in 1 patient. These symptoms were controlled by reducing aspirin dosage and lowering the serum salicylate level. The "special salicylate syndrome" of mental confusion, dehydration, and hyperventilation associated with a respiratory alkalosis was observed in mild form in one patient; signs and symptoms disappeared when aspirin was withdrawn. During salicylate therapy 12 of the 14 patients noticed varying degrees of impaired hearing, which reverted to normal after administration of the drug was discontinued. Tinnitus occurred in 7 patients but tended to disappear spontaneously as time went on. The reported data place salicylate in the class of promising orally administered antidiabetic substances; they should stimulate investigations to remove the undesirable effects of the drug and to find out its mechanism of action.

Combined Treatment with Emetine and Chloroquine of Amebic Hepatitis: Elective Indications and Advantages. V. Scaffidi and R. Astuto. Minerva med. 50:317-324 (Feb. 7) 1959 (In Italian) [Turin, Italy].

The authors report on the effect of emetine combined with chloroquine in 6 male patients with amebic hepatitis. The first patient, who was 58 years of age, was observed on the 9th day after the onset of a markedly progressive hepatitis, which discouraged the administration of adequate quantities of emetine because of marked toxic infectious symptoms and hypotension which also caused gastric intolerance to chloroquine. One cycle of treatment with low doses of both drugs had a good rapid effect: a remission of the symptoms followed soon; aspiration puncture of the liver was not necessary; erythrocyte sedimentation rate became normal in a short period of time; the patient recovered, and no further treatment was necessary. The second patient, who was 70 years of age, had been suffering from hepatitis for 3 months; his general condition was poor; he had fever, anemia, hypotension, and tachycardia. Complete recovery was obtained after 11 days of treatment with total doses of 0.44 Gm. of emetine and 6 Gm. of chloroquine; the latter drug was given for 8 days only. The erythrocyte sedimentation rate dropped before completion of the treatment. The remaining 4 patients, 44, 51, 60, and 36 years of age, respectively, were treated with emetine given in a similar dose as in the 2 previous cases; chloroquine was given in a dose of 1 Gm. per day. Three of these patients improved rapidly and recovered completely after only one cycle of treatment. The 4th patient recovered more slowly; no relapse of hepatitis was observed a few months later when the patient suffered from an episode of persistent ulcerative colitis, which was cured with emetine combined with Aureomycin. The emetine-chloroquine treatment had no untoward side-effects.

The Use of Chlorothiazide in the Nephrotic Syndrome. G. E. Burch and H. A. White Jr. A. M. A. Arch. Int. Med. 103:369-380 (March) 1959 [Chicago].

Chlorothiazide is a new diuretic agent which is useful in the treatment of many clinical disorders, including congestive heart failure, cirrhosis, nephrosis, essential hypertension, premenstrual edema, and toxemia of pregnancy. Among its various clinical advantages are (1) remarkable effectiveness when administered orally and (2) prompt diuretic action, consisting of water diuresis, natruresis, and chloruresis but only minimal kaluresis. Chlorothiazid is twice as potent as acetazolamide. The authors studied 10 patients with the nephrotic syndrome associated with various types of renal disease; these patients received oral treatment with chlorothiazide at the Charity Hospital of Louisiana in New Orleans between 1955 and 1957. The diet of all patients contained a constant known intake of electrolytes (1.5 Gm. of sodium) and of protein (78 Gm.).

Chlorothiazide proved to be an effective, and sometimes dramatic, diuretic agent. Six of the 10 patients had the classical picture of the nephrotic syndrome with edema and were refractory to conventional therapy. The response to chlorothiazide in these patients was striking. One of these patients, a 16-year-old girl with proliferative and membranous glomerulonephritis, generalized edema, and ascites, failed to respond to conventional therapy. The patient was then given 0.5 Gm. of chlorothiazide twice daily, resulting in a loss of weight of 24 lb. (11 kg.) within 9 days and a considerable improvement of well-being. She was discharged edema-free, on a maintenance dose of 250 mg. of chlorothiazide daily. When seen 3 months later, she had no edema or evidence of electrolytic imbalance, although the condition of the urine and hypoproteinemia were unchanged. In another patient who had severe diabetic glomerulosclerosis, the diuretic response to the first course of chlorothiazide was better than the response to a single injection of a mercurial diuretic. The diuresis was accompanied by a pronounced increase in urinary excretion of sodium and chloride but a minimal increase in excretion of potassium.

In 9 patients studied before and during chlorothiazide therapy, the mean daily excretion of sodium increased from 122 to 200 mEq. per liter, of chloride from 118 to 188 mEq., and of potassium from 45 to 58 mEq. The rates of plasma clearance for sodium, chloride, and potassium were higher in all the patients during administration of chlorothiazide than were the control values, with occasional exceptions when a mercurial diuretic was used. The total quantity of sodium excreted during therapy with chlorothiazide far exceeded that of potassium. The creatinine clearances of all the patients remained essentially unchanged throughout the entire study, indicating no significant change in glomerular filtration. Although the urinary volumes in these patients increased at the time of administration of chlorothiazide, they lost relatively greater quantities of electrolytes than of water, and the specific gravity of their urine was 1.012 or greater.

Although renal biopsies have not been repeated, no evidence was found that chlorothiazide had any detrimental effect on the basic renal lesion. This drug appeared only to promote diuresis and to produce dry weight. This, in turn, had considerable psychological and clinical benefit for the patients who had been edematous for long periods of time despite other intensive therapy. All edema was eliminated in these patients by oral treatment with chlorothiazide, except for facial edema associated with steroid therapy in 2 patients.

Developments in Fibrinolytic Therapy for Thrombo-Embolic Disease. S. Sherry, A. P. Fletcher and N. Alkjaersig. Ann. Int. Med. 50:560-570 (March) 1959 [Lancaster, Pa.].

Considerable progress has been made in developing systemic fibrinolytic therapy for use in man. The naturally occurring precursor of the fibrinolytic enzyme of serum is referred to as plasminogen or profibrinolysin. In the presence of a kinase or activator, this normal serum globulin is converted to plasmin or fibrinolysin. Streptokinase, a hemolytic streptococcic product, is the best-known of the activators and has been used in most laboratories. Plasmin, also to be referred to as fibrinolysin, is a proteolytic enzyme. Although plasmin digests fibrin into several soluble polypeptides, this proteolytic enzyme is capable of digesting such additional plasma constituents as fibrinogen, accelerator globulin, and some of the components of serum complement. Free plasmin in blood is rapidly inhibited by antiplasmins found in serum and platelets. Plasminogen is closely related to fibrinogen and fibrin. Plasminogen and fibrinogen appear simultaneously in areas of exudation, and significant amounts of plasminogen are adsorbed onto fibrin during clotting. This close relationship is probably of physiological significance.

In discussing the mechanism by which a thrombus is lysed, the authors point out that the level of activator in the circulation, rather than the level of circulating fibrinolysin, becomes the critical factor in controlling the rate of lysis of a thrombus. The importance of plasminogen in the circulation is not to induce fibrinolysis but to endow thrombi or fibrinous exudate with sufficient plasminogen to mediate its lysis.

To test this hypothesis, a study was conducted on patients subjected to procedures known to enhance the fibrinolytic activity of the blood. It was possible to demonstrate that, after electroshock, pyrogen therapy, ischemia, exercise, and epinephrine injections, the enhanced fibrinolytic activity was associated with the release of activator in, or into, the circulation; yet there were no significant changes in the plasmin or the fibrinogen concentrations of the plasma. Four methods of fibrinolytic therapy were considered: (1) the use of pharmacological agents capable of influencing the release of the physiological activator; (2) the use of purified preparations of known activators; (3) the use of purified preparations of human plasmin; and (4) the use of other proteolytic enzymes capable of hydrolyzing fibrin, e. g., trypsin and chymotrypsin.

Direct control of the circulating activator level may be accomplished by prolonged infusions of large amounts of highly purified activator preparations. Although urokinase, an activator derived from human urine, probably would be most desirable for this purpose, it is not yet available in pure form, and a highly purified streptokinase has been used. Therapy has been instituted by the intravenous injection of a priming dose of streptokinase, dependent in amount upon the level of circulating antibody and varying between 10,000 and 200,000 units. Thereafter, the level of circulating activator has been maintained by a sustaining infusion of 30,000 to 100,000 units of streptokinase an hour. This regimen, based on studies with isotopically labeled streptokinase, maintains a plasma level of from 3 to 10 streptokinase units per milliliter.

The more than 50 patients treated by this technique included some with acute coronary thrombosis and myocardial infarction, deep vein thrombophlebitis with and without complicating pulmonary emboli, thrombotic occlusions of large arteries, and arterial and venous occlusions of retinal vessels. Evidence has been obtained in some instances that intravascular fibrinolysis has been produced. Other activators, e. g., urokinase, may prove to be less antigenic and more useful than streptokinase, or perhaps pharmacological methods for controlling the natural activator level may be developed.

Clinical Evaluation of Formamidinyliminourea, a New Biguanide Oral Blood Sugar Lowering Compound: Comparison with Other Hypoglycemic Agents. L. P. Krall and R. F. Bradley. Ann. Int. Med. 50:586-613 (March) 1959 [Lancaster, Pa.].

The search for orally effective hypoglycemic agents preceded the advent of insulin; it began in 1914 when it was discovered that hypoglycemia was accompanied by increased levels of guanidine in the blood and that the administration of guanidine produced hypoglycemia. Further study of guanidine derivatives led to the finding of a higher homologue, Synthalin, a decamethylene-diguanidine, which produced hypoglycemia in normal and in diabetic dogs after parenteral or oral administration. Synthalin decreased glycosuria in human diabetics, and clinical success in some mild and moderately severe diabetic patients was reported. While Synthalin was being used by many investigators, insulin was assuming its physiologically sound position in diabetic treatment. The authors discuss the metabolic effects and the action mechanism of Synthalin and compare it with a new series of orally administered hypoglycemic agents known as biguanides or formamidinyliminoureas.

The present report evaluates the clinical characteristics of 4 biguanide analogues. These are DBI, the phenethylformamidinyliminourea, and the closely related derivatives: DBB, the normal amyl; DBTU, the isoamyl; and DBC, the methylbenzyl analogue. Certain parallels and differences between these compounds in terms of chemistry, metabolic effects, side-effects, and possible sites of action are noted. The toxicity reported with guanidine and Synthalin has not occurred to date in experimental or clinical observations with the biguanides. Effects of biguanides used for varying periods of time up to 17 months were evaluated in 173 patients with all types of diabetes, including 53 juvenile-onset cases. Duration of diabetes was from newly diagnosed to 35 years. Of the study group, 150 patients (88%) showed demonstrably lowered blood sugar levels, while 66 (38%) were unable to continue biguanide therapy because of gastrointestinal side-effects in the doses used. Although gastrointestinal side-effects occurred frequently, they were rapidly reversible. No clinical toxicity was noted. Hepatic, renal, and hemotological studies have revealed no abnormality to date. The long-term effects of the biguanides are still to be determined. Comparison with other hypoglycemic agents suggests that, when used with certain precautions, they have clinical value in selected cooperative patients.

The Artificial Kidney. F. M. Parsons and B. H. McCracken. Brit. M. J. 1:740-751 (March 21) 1959 [London].

The authors report on 100 patients who were referred to the artificial kidney unit of the General Infirmary at Leeds, England. Of the 100 patients, 63 had acute reversible renal failure which occurred as a complication of pregnancy in 25, as a result of or associated with trauma in 25, and from other causes in 13; 13 patients had acute irreversible renal failure; 13 patients had postrenal obstruction which was reversible in 9 and irreversible in 4; and 11 patients had miscellaneous condtions, 9 of whom had an exacerbation of chronic renal disease. Eighty-two of the 100 patients underwent hemodialysis with an improved Kolff-Brigham rotating type of artificial kidney. Of the 63 patients with acute reversible renal failure, 45 were dialyzed. There were 24 female and 21 male patients, between the ages of 13 and 67 years. The basic treatment was a dietary regimen consisting of 400 cc. of water and 100 Gm. of dextrose daily, with vitamins. The most consistent indication for dialysis was clinical deterioration, particularly early mental changes, nausea, and vomiting. The biochemical indications were a blood urea nitrogen level of 180 to 200 mg. per 100 cc., a potassium level of 7 mEq. per 1,000 cc., and a carbon dioxide combining power of 13 mEq. per 1,000 cc.

The metabolic response, estimated by the daily rise of the blood urea nitrogen level, was remarkably constant in any one patient, and a classification of the illness into mild (rise less than 15 mg. per 100 cc. a day), moderate (rise of 15 to 30 mg. per 100 cc. a day), and severe (rise of 30 mg. or more per 100 cc. a day) is suggested. The patients with mild illness were frequently managed successfully without dialysis, while those with moderate illness (mainly those with complications of late pregnancy) usually required a dialysis between the 6th and the 10th day. The patients with severe illness (mainly those with renal failure associated with trauma, accidental or surgical) often required dialysis as early as the 4th or 5th day. In the patients with severe illness the incidence of complications, particularly sepsis, was high and the mortality greater. Many of these patients were referred to the artificial kidney unit too late; earlier transfer might improve the prognosis.

The metabolic response in women with acute reversible renal failure occurring as a complication of pregnancy was reduced by 70% when the patients were given 30 mg. of norethandrolone (Nilevar) daily. Administration of this steroid might largely eliminate the need for dialysis in pregnant women. A similar action has not been observed in other conditions. Of 9 patients with reversible postrenal obstruction and uremia who were dialyzed, 7 had prostatic obstruction with retention of urine. After dialysis all were improved clinically. In 3 of the 7 patients, prostatectomy was performed 7 days or less after the dialysis, but in the other 4 prostatectomy had to be delayed until renal function had improved, and in 1 of these 2 further dialyses were required. The number of patients with chronic renal failure referred to the artificial kidney unit was too small for justifiable conclusions to be drawn. In those patients with acute renal failure of not clearly understood origin, dialysis was used so as to maintain life while diagnostic procedures were undertaken. If an irreversible condition was found, no further dialyses were performed.

Streptomycin Poisoning in Renal Failure: An Indication for Treatment With an Artificial Kidney. K. D. G. Edwards and H. M. Whyte. Brit. M. J. 1:752-754 (March 21) 1959 [London].

Three men, between the ages of 28 and 68 years, and 2 56-year-old women who had been treated with a total dose of streptomycin varying from 4 to 14 Gm. for recurrent pyelonephritis or for postoperative prophylaxis after an orthopedic operation and a thoracotomy, respectively, were observed at the Sydney (Australia) Hospital in the past 2 years. All had permanent vestibular damage and evidence of renal disease. In 2 patients with acute oliguric renal failure, the symptoms of vestibular damage appeared 24 days after the administration of the last dose of streptomycin and after diuresis had occurred. A simple, semiquantitative, in vitro test showed that streptomycin can be removed from the blood by dialysis. These observations induced the authors to give hemodialysis a trial in 3 women and 2 men, between the ages of 30 and 62 years, with acute renal failure who had received 1.5 to 10 Gm. of streptomycin for prophylaxis after surgical intervention and for septicemia respectively. Hemodialysis was performed as early as possible, within 3 to 9 days after the institution of streptomycin therapy. Signs of toxicity did not occur in any of these patients. Accumulating experience emphasizes the importance of estimating renal function before giving a course of streptomycin. There is every reason to believe that early removal of streptomycin, which is confined to the extracellular fluid in the body, by dialysis should assist in preventing vestibular damage. Administration of streptomycin in patients with renal failure is to be considered one of the few conditions calling for immediate treatment with an artificial kidney.

PHYSIOLOGY

Agammaglobulinemia and Alymphocytosis with Atrophy of the Lymphatic Tissue. W. H. Hitzig, Z. Biro, H. Bosch and H. J. Huser. Helvet. paediat. acta 13:551-585 (Dec.) 1958 (In German) [Basel, Switzerland].

The distinction between cellular and humoral defense mechanisms has become better understood since discovery of patients with agammaglobulinemia made possible a better evaluation of humoral factors. The authors present the histories of 2 male infants who had an especially low resistance to infection. This was the result of a double defect, namely, an absence of humoral antibodies (agammaglobulinemia) and of cellular elements (alymphocytosis). The clinical course was, therefore, extremely unfavorable and proved more resistant to therapy than is usually the case in agammaglobulinemia. The insufficiency of the 2 important defense mechanisms revealed the following characteristics in the 2 infants: 1. Onset was toward the end of the first 3 months of life. 2. Severe diarrhea which proved resistant to all therapy resulted in severe cachexia. 3. There was persistent lowering of the lymphocyte count, although the total number of leukocytes and of neutrophils varied. (4) Gamma globulin values in the blood were extremely low, and specific antibodies and isoagglutinins were absent. 5. Allergic reactions were the same as in normal persons. One patient died of a hemolytic–uremic syndrome with all the characteristic features of the generalized Sanarelli-Shwartzman phenomenon. The other patient had a severe neurological disorder (hemiplegia). Autopsy studies on both infants revealed that the entire lymphatic system was atrophic.

The authors feel that the cases presented are important for evaluation of the relations between cellular and humoral defense mechanisms. Contradictory opinions have been expressed about the site of origin of the humoral antibodies. According to the lymphocytic theory it is deduced from antibody determinations in lymph and in lymphocytes that the latter contain and transport antibodies. However, histological studies on stimulated lymph nodes indicate a secretion of antibodies by sessile elements, that is, by activated reticulum and plasma cells. Two refined modern techniques permit corroboration of the plasma-cell theory. The gamma globulins can be demonstrated in plasma cells with the aid of fluorescent anti-gamma-globulin serums and with the electron microscope. It can be demonstrated that plasma cells have an ergastoplasm, that is, a highly organized system of intracellular concentric membranes and granules; lymphocytes and the plasma cells of the peripheral blood do not have them. It can also be demonstrated how the plasma cell achieves contact with the corresponding antigen. Plasmatic protrusions of macrophages that contain the antigen reach into kidney-shaped invaginations of the plasma cells; at the sites of contact the membrane becomes very thin, so that the organelles of the plasma cell are enabled to "palpate" the surface of the antigen. A plasma-cell theory of the formation of antibodies is formulated on the basis of these observations.

Electrocardiograms of Weight-Lifters: Study of Findings of 26 Subjects. R. Etzenhouser, M. Dunn and E. G. Dimond. J. Kansas M. Soc. 60:121-125 (March) 1959 [Topeka].

The weight-lifter is an example of a highly conditioned athlete in whom the demands on the cardiovascular system are just the opposite of the usual requirements of physical fitness. Practically all other physical fitness sports require sustained demands on cardiac output by increasing stroke volume and heart rate. The weight-lifter does immense physical work while performing a Valsalva maneuver. The weight-lifter impedes venous return, decreases cardiac filling, and decreases cardiac output at the same moment he exerts maximal effort. The authors made electrocardiographic studies on 26 male weight-lifters, ranging from 16 to 40 years of age. These men had been weight lifting from 4 months to 10 years for 1½ to 20 hours per week. Preliminary examination consisted of obtaining a medical history, weight-lifting history, blood pressure, and auscultation of the heart. A standard 12-lead electrocardiogram was then taken on each subject, who next completed 50 trips over the standard Master 2 steps in 3 minutes. Immediately after exercise, leads I, II, III, V_4, V_5, and V_6 were taken and repeated at 2-, 4-, and 6-minute intervals thereafter.

Three of the 26 subjects had abnormal exercise electrocardiograms. An arrhythmia developed after exercise in one man; another one before exercise had T-wave inversion which reverted to normal immediately after exercise; and in a third man there developed a terminal depression of the S-T segment with inversion of the T waves. Only the changes developing in the last of these 3 men could be interpreted as possibly demonstrating myocardial ischemia. The T-wave inversion noted in the one man at rest is of the innocent variety, since it has been produced in young adults by many factors, including emotional stress, autonomic dysfunction, and a full stomach. The authors conclude that the electrocardiographic changes were probably physiological adaptations well within the capacities of the normal heart.

BOOK REVIEWS

Treatment of Cancer and Allied Diseases. Volume II: Tumors of the Nervous System. By thirty authors. Edited by George T. Pack, M.D., F.A.C.S., Attending Surgeon, Memorial Center for Cancer and Allied Diseases, New York, and Irving M. Ariel, M.D., F.A.C.S., Associate Clinical Professor of Surgery and Associate Attending Surgeon, New York Medical College, Flower and Fifth Avenue Hospitals, New York. Second edition. Cloth. $15. Pp. 316, with 340 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1959.

The first edition of this book appeared in 1940. The present edition contains much useful information, and the authors selected to prepare the various sections are among the most outstanding authorities in the United States. Unfortunately outdated material has not been entirely eliminated, and the book has not been completely modernized. Few if any neurological surgeons would today use the surgical approach for an acoustic neuroma illustrated in figure 1-15, page 12, or in figure 11-5, page 164. Figure 1-17, page 13, gives a most inadequate idea of the procedure of cerebral lobectomy. Not many surgeons would curve the incision for a subtemporal decompression forward, as shown in figure 1-20, page 16. In discussing the prognosis of the treatment of the benign astrocytomas of the cerebellum it should be pointed out that most of these patients can be permanently cured if they are properly treated. There are numerous other points to which one might take exception. In too many instances one finds the subject matter superficially dealt with, particularly the subject of prognosis. On the other hand, chapter 3 on anesthesia, chapter 4 on preoperative and postoperative care, and chapters 18 and 19 on tumors of the peripheral and sympathetic nervous systems are well written. Chapter 10 on the treatment of intracranial meningiomas is one of the best in the book. While the bibliography is poorly arranged, the index is adequate.

History of the Second World War: United Kingdom Medical Series. Editor-in-chief: Sir Arthur S. MacNalty, K.C.B., M.A., M.D. The Army Medical Services: Campaigns. Volume III: Sicily, Italy, Greece (1944-45). By F. A. E. Crew, F.R.S. Cloth. 100 shillings. Pp. 645, with 136 illustrations. Her Majesty's Stationery Office, Atlantic House, Holborn Viaduct, London, E. C. 1, England, 1959.

This third volume of the history of the medical service of the British Army in World War II deals with both the preparations for and the actual invasion of Sicily, Italy, and Greece. Although military strength and effectiveness in these campaigns were more gravely threatened by disease than by enemy action, a high standard of health promotion, disease prevention, and individual treatment was reached. In Italy malaria, venereal disease, dysentery, typhoid, and typhus were all prevalent. These hazards were aggravated by the fact that the troops were often exposed to rain, snow, and wide variations in external temperature. Furthermore they moved amid a teeming civilian population whose social and economic life had been disrupted by the war. Long periods away from home had a deteriorating effect on the morale of the troops, thereby decreasing their attention to personal hygiene and increasing their susceptibility to disease.

Although this volume is generally well written, it contains a superabundance of tactical details which are not of general interest. The appendixes, 26 in all, are scattered throughout the book at the end of individual chapters rather than being all placed at the end of the book. In the front there is an extensive list of abbreviations without which the book would be unintelligible. Even so, there are a few omissions, probably of those abbreviations already familiar to most British readers. There are many photographs, but most of the illustrations are simple maps. There is an index. Those in the United States who have a special interest in military medicine should find it interesting to compare the British procedures and conclusions with those of our own forces regarding the campaigns in these countries.

Neoplastic Disease at Various Sites. Volume II: Tumours of the Bladder. Edited by David M. Wallace, O.B.E., M.S., F.R.C.S. General editor: D. W. Smithers, M.D., F.R.C.P., F.F.R. Cloth. $11.50. Pp. 352, with 202 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland, 1959.

This is one of many monographs on neoplastic diseases published under the general editorship of Dr. Smithers. There are 14 contributors. As monographs go, this volume is exceedingly large, but it is by far the best publication on bladder tumors available. The publishers have done an excellent job in that the paper is of high quality, the print is easy to read, and the illustrations, charts, graphs, photographs, photomicrographs, and colored plates are excellent.

The contributors have presented their various topics in a clear, concise, and informative style. The book is "all meat." Each chapter is well arranged, and many have conclusions (all have references at the end). Too much has been written about cancer without a clear definition of what is to be discussed. The industrial risk in the development of certain bladder tumors has been recognized for some years. Although formerly described as aniline dye cancers, it is now recognized that these neoplasms can be

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

produced by many chemicals similar in every respect to those that appear spontaneously. In spite of all modern advances in treatment the mortality from bladder cancer is rising. These facts and many others, including etiology and biochemistry, are presented in the first three sections.

There is a large section on the pathological behavior and the mode and method of spread of bladder cancer. There is also an analysis of postmortem findings and manner of death. The last three sections contain discussions of the classifications, methods of treatment, analysis and result of treatment, and an appraisal of the various methods. The observations on treatment as presented confirm those of Jewett, in that once the bladder musculature has been penetrated the chances of cure diminish rapidly. The book has an excellent appendix which includes many interesting charts and statistics. The whole subject of bladder tumors, including classification and treatment, is controversial. There are those who will take exception to some of the opinions expressed in a few of the chapters. A few may even believe that some of the subject matter has been treated too superficially. Be this as it may, the monograph can be highly recommended not only to the urologist but to the radiotherapist, industrial chemist, investigator, and anyone else enterested in cancer.

Chirurgie der Arterien. Von Doz. Dr. K. Kremer. Mit einem Vorwort von Prof. Dr. Ernst Derra. Cloth. 59 marks; $14.05. Pp. 280, with 150 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

This is a purely technical treatise on the surgery of blood vessels, including a short history of vascular operations and a description of instruments; homograft, heterograft, and plastic transplants; and the treatment of various forms of visceral and peripheral arterial syndromes. There is a short chapter on diagnostic methods. Photographs are well reproduced, but many of the diagrams are too small and too sketchy. The material is well organized and the bibliography is extensive. For the German-speaking surgeon, the book offers a good summary of present concepts. One may note with pride that most of the recent developments in this field come from English or American sources. There is little to recommend it for the reader in this hemisphere.

Surgical Treatment of Mitral Stenosis. By Helge Baden. [Thesis, M.D. University of Copenhagen.] Translated from Danish by Axel Andersen. Paper. 20 Danish kroner. Pp. 263, with 17 illustrations. Store Nordiske Videnskabsboghandel, Copenhagen, Denmark, 1958.

This monograph analyzes a series of 165 patients treated by mitral commissurotomy and compares it with other series reported in the literature. The monograph begins with a comprehensive but concise review of the literature. The symptoms, clinical findings, and laboratory findings are discussed in detail, with tables and graphs to illustrate important factors. Operative technique is described, with details of the findings at operation and the complications that arose. The operative mortality of 10% is analyzed and details of postoperative complications are given. Comparison of the diagnostic and operative findings is made with special reference to the degree of stenosis and the amount of regurgitation. Postoperative results are reported objectively with 52% of the patients improved, 26% unchanged, 6% worse, and 16% dead. Factors influencing these results are analyzed. A comprehensive bibliography is included.

Radiation Biology and Cancer: A Collection of Papers Presented at the Twelfth Annual Symposium on Fundamental Cancer Research, 1958. Published for University of Texas M. D. Anderson Hospital and Tumor Institute. Cloth. $8.50. Pp. 493, with illustrations. University of Texas Press, Austin 12, 1959.

This book contains a series of papers reporting studies on the physical and chemical aspects of radiation and radiobiology encountered in investigations of the cause and treatment of malignant disease. Observations of a preliminary nature which call attention to the basic factors involved in these problems are presented. The book should serve as a reference point for critical students in the fields of radiation and cancer, but it may not find general acceptance by the average reader, since the material is highly specialized. The fact that the book reveals important vistas of this complex subject may result in a future stream of publications on many of the challenging aspects of the problem.

Bronchography. By C. Dijkstra, M.D., Medical Superintendent of "De Klokkenberg," sanatorium and chest hospital, Breda, Netherlands. Translated from Dutch manuscript by Th. R. Heemskerk. Cloth. Hfl. 19.50. Pp. 157, with 106 illustrations. Koninklijke van Gorcum & Co. N.V., Assen, Netherlands; Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1959.

Reading the title of this book, published so many years after the development of this diagnostic method, one wonders what it can add to what is common knowledge. This question the author has carefully considered and well answered in his preface. Inasmuch as this procedure is increasingly recognized as a necessary part of a complete study of the lungs, and inasmuch as it is being used more and more by those who have not had extensive experience with it, a monograph of this type, which describes the technique of injecting the oil and the interpretation of the bronchograms, is definitely needed. There is much in the book that should add to the knowledge even of those who have wide experience with bronchography. It should, therefore, be of great value to the less experienced. The text is brief but well written and adequate. The illustrations are numerous and excellent, and the author's method of using case histories to present the diagnostic pictures is well adapted to this subject.

Praktische Anatomie: Ein Lehr- und Hilfsbuch der anatomischen Grundlagen ärztlichen Handelns. Erster Band/dritter Teil: Arm. Von Dr. T. von Lenz, o. ö. Professor der Anatomie, Direktor des Anatomischen Institutes der Universität München, und Dr. W. Wachsmuth, o. ö. Professor der Chirurgie, Direktor der Chirurgischen Universitätsklinik und Poliklinik, Würzburg. Second edition. Cloth. 168 marks. Subscription price 134.40 marks. Pp. 308, with 249 illustrations. Springer-Verlag, Heidelberger Platz 3, (1) Berlin-Wilmersdorf (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1959.

This monograph on the upper extremity is part of a series of comprehensive works designed to present the anatomic basis of medical practice to the physician. In 1935 the first edition on the upper extremity appeared, followed in 1939 by a volume on the leg. The first postwar production by the anatomist von Lanz and the surgeon Wachsmuth was the volume on the neck, published in 1955. The present work is a thoroughly revised edition of the initial publication in the series. Monographs on the practical anatomy of the head, thorax, back, abdomen, and pelvis will complete the series. The volume on the arm has been reissued prior to the completion of the other proposed volumes, partly because of the intense interest in the reconstructive surgery of the hand. Destruction of the plates, drawings, and most of the printed stocks in World War II necessitated the preparation of what is in reality an entirely new edition.

As in other works in the series the anatomy of the upper extremity is presented chiefly from the regional, topographical, and functional points of view. Systematic presentation is used to a lesser degree to supplement the more practical regional approach. The aim throughout is to set forth the anatomy of the living as the foundation of medical practice in general and of surgery in particular. The illustrations, mostly in color, are large and their abundance permits the careful study of a part or an area without the confusion of a multitude of leaders and labels, as is often the situation when illustrations are few in number. Numerous "phantom" drawings are used to illustrate surface projections and relations. Neurovascular variations and their relations to muscular and bony structures are also discussed and illustrated.

A general section on the upper extremity as a whole precedes detailed accounts of the several subregions. About 70 pages are devoted to the hand. In each subsection surface anatomy, illustrations of successively deeper dissections, cross-sections, movements, joints and ligaments, muscular and bony relations, variations and anomalies, and practical applications are presented. A comprehensive list of references and a detailed index are provided. The new anatomic nomenclature (*Nomina Anatomica Parisiensia*, 1955) has been incorporated into the text. There are no illustrations of the radiologic appearance of the anatomy of the upper extremity. The type face is large, clear, and easy to read. The cover and binding appear to be sturdy and durable. It is difficult to compare this work with any other since it is unique in its comprehensiveness, and in the abundance, clarity, and general excellence of its illustrations. Although it is written in German, this fact only slightly diminishes its usefulness to a nonreader of the language. This book can be recommended without reservation to the general physician, but more specifically to the surgeon. Medical and anatomic libraries should find this an excellent addition to their reference collections.

Recent Trends in Chronic Bronchitis. Edited by Neville C. Oswald, T.D., M.D., F.R.C.P. Cloth. $7.50. Pp. 199, with 174 illustrations. [Oxford University Press, 114 Fifth Ave., New York 11]; Essential Books, Fair Lawn, N. J.; Lloyd-Luke (Medical Books) Ltd., 49 Newman St., London, W. 1, England, 1958.

The editor states that the main purpose of this book is to bring together under one cover for the first time recent views on the various facets of chronic bronchitis. Much of the text consists of the original work of several contributors. From their experience with chronic bronchitis at Brompton Hospital since 1950 the authors present their views on the diagnosis, prevention, and treatment of this distressing and often killing disease. The book begins with a discussion of the mortality and morbidity of chronic bronchitis and proceeds to the clinical pattern of the disease, which is discussed at some length. There is an excellent chapter on pathology, giving a historical review and following it with a discussion of the normal anatomy of the bronchial tree, before going into the pathological findings of the disease throughout its course. There are some excellent colored pictures of pathological slides as well as many pertinent illustrations in black and white. Other chapters discuss the radiologic appearance of the chest, the bacteriology of the disease, the effect of air pollution, the disturbances of respiratory function and of the heart in chronic bronchitis, and emphysema. The clinical management and the aspects of bronchitis in general practice are dealt with in the last chapters. References are given at the end of each chapter and there is a good index.

Each chapter is well written. This book is not meant to be an exhaustive treatise but rather a summary of the experiences and the conclusions of the group studying chronic bronchitis at Brompton Hospital. In this respect it fulfills its purpose, and it should be enjoyed by many students and general practitioners of medicine.

QUESTIONS AND ANSWERS

RECURRENT FURUNCULOSIS

To the Editor:—*A 33-year-old man started to have boils about four months ago, all of them below the level of the waistline. They have been painful and resistant to antibiotic treatment. Most of them need to be incised. All the conventional treatments have failed. A culture revealed Staphylococcus aureus. Please give advice on treatment.*

Juan Ferrando, M.D., Lima, Peru.

Answer.—The management of recurrent furunculosis should be directed not only to cure the local lesions but also to prevent recurrences by attention to the source of the infection and to the mode of transfer. The furuncles themselves require proper surgical drainage, compresses, and proper dressings. Careful cultural studies should be made to determine the exact strain of the offending organism and its drug sensitivity. Combined treatment should then be directed toward complete eradication of the lesions at all points by systemic use of the indicated antibiotic as well as by frequent skin cleansing with soap and water or with a detergent such as hexachlorophene, which leaves a thin skin film to suppress bacterial growth. Sources of chronic infection about the perineum and anus are likely to promote recurrent furunculosis, and these should be eradicated surgically or medically. The hands and undergarments should be scrupulously cleaned at frequent intervals. The anatomic distribution suggests a chronic source of infection about the perineum or anus, and particular attention must be given to the underclothing and to the hands.

CALORIE EXPENDITURE

To the Editor:—*How many calories are expended by a person weighing 150 lb. (68 kg.) walking one mile at the rate of 3 mph?* *M.D., New York.*

Answer.—According to studies reported by the Army Medical Nutrition Laboratory, the calorie cost of a man weighing 70 kg. walking on the level at a rate of 3½ mph is 5.25 per minute. Assuming the energy expenditure to be approximately the same at a rate of 3 mph, walking one mile would expend 105 calories. Further details regarding other factors that may be concerned can be obtained from the "Medical Nutrition Laboratory Report No. 177" (Denver, Fitzsimons Army Hospital, March 19, 1956). Lusk's book "Elements of the Science of Nutrition" (ed. 4, Philadelphia, W. B. Saunders Company, 1928) states that the extra energy required for walking 2.8 mph for one hour is 159 calories above the resting dietary requirement. This is equal to 17.1 Gm. of fat. The resting calorie requirement is about 40 calories per square meter per hour, and a 150-lb. man would have approximately 1.65 square meters of surface area, requiring 66 calories per hour or a total energy production of 225 calories per hour while walking 2.8 mph. This would give 75 calories as the energy expenditure for walking one mile. The more recent data are probably more representative of current techniques, which are more refined than those used when the early data given by Lusk were obtained.

TUBERCULOUS TONSILLITIS

To the Editor:—*In a patient with tuberculous tonsillitis, should tonsillectomy be performed? A 28-year-old man developed a sore throat in December, 1958. Three weeks later he noted a lump in the right side of his neck. On physical examination his right tonsil was three times as large as the left and dark red and there was a lump in the upper portion of the right side of the neck. His temperature was 38 C (100.4 F). He was hospitalized, and the lump grew larger, with a chain of tender nodes extending to the supraclavicular region. The leukocyte count was 4,000 per cubic millimeter. His fever persisted in spite of tetracycline, sulfonamides, and penicillin therapy. A biopsy specimen of the right tonsil revealed a tuberculous lesion. The patient is ambulant.*

V. A. Mandrussow, M.D., San Francisco.

Answer.—The inquirer seeks help for the treatment of an acute case of tuberculous tonsillitis, but his description of the case casts some doubt on this diagnosis. The marked enlargement of the right tonsil and its association with chain-like nodes extending to the supraclavicular region is more suggestive of malignant lymphoma, possibly of the Hodgkin's type. A blood dyscrasia must be considered in view of the low leukocyte count, and a differential count is indicated. A review of the original biopsy specimen is also in order. If this is indeterminate, excision biopsy of the tonsil and one of the cervical nodes is recommended.

Acute tuberculous tonsillitis is rare and seen only in association with pulmonary tuberculosis. It is accompanied by exudation and ulceration, and the

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patient is usually very ill. The possibility of latent tuberculosis of the tonsil associated with cervical adenopathy must undoubtedly be considered. This was formerly attributed to the bovine type of tuberculosis and has almost disappeared in recent years. The cervical node biopsy should be helpful in this determination. The mere finding of a tuberculous lesion of the tonsil on histological examination is of no great significance. Routine studies of excised tonsils may occasionally reveal this in the absence of clinical evidence of the disease. Other granulomatous diseases may produce lesions resembling tuberculosis. Tonsillectomy in this case can be recommended for diagnostic rather than therapeutic reasons.

"BODY WISDOM" DEFECT

To the Editor:—*It is understandable that one perspires when shock is due to toxemia or poisoning, but what happens to the "wisdom of the body" when the shock is due to hemorrhage or coronary thrombosis?* *M.D., New York.*

Answer.—Sweating is produced by stimulation of the cholinergic fibers present in sympathetic nerves. In shock due to hemorrhage or acute coronary occlusion, there is stimulation of the vegetative nervous system. Some of the manifestations reflect the effects of adrenergic stimulation, while other effects are typical of a cholinergic response. It is doubtful whether many of the physiological adjustments to shock are sufficiently well understood for their significance to be appreciated. Presumably, the loss of fluid by perspiration would be undesirable, but some other cholinergic effects may be essential to maintaining vital functions of the circulation. There are numerous instances in which the body does not manifest "wisdom." For example, nontoxic substances may be metabolized into toxic substances. Phagocytic cells may help disseminate infections, such as tuberculosis.

HOT WEATHER FATIGUE

To the Editor:—*What is the cause of fatigue—not discomfort—during hot weather in the summer? Is it metabolic in origin?* *M.D., New York.*

Answer.—Several factors may contribute to a sense of fatigue during the hot summer weather. These may include a general relaxation of musculature and vasodilatation, as well as electrolyte loss through perspiration. The increased vasodilation required for heat dissipation in hot weather may tend to reduce blood flow through the muscles and viscera. The altered distribution of blood flow could be a factor in producing fatigue. It is not clear to what extent the weather may influence endocrine function, but there is some reason to believe that a cold environment may tend to stimulate adrenal cortical function. Metabolism tends to be at a minimum as the environmental temperature approaches that of the body. It is hard to distinguish between physiological and psychological factors that may enter into such a complaint. There is no evidence that this form of fatigue is metabolic in origin in healthy subjects.

TREATMENT OF RESPIRATORY INFECTION AND FEVER IN A CHILD

To the Editor:—*What is the present opinion regarding treatment for a child 10 years of age with fever and a sore throat or, shall we say, any upper respiratory infection with fever in a child? Years ago early treatment was advocated as a means of aborting the illness and preventing septic complications. Recently one hears more and more of the value of letting the child handle the infection without benefit of antibiotics in order to develop antibodies. What is considered good practice today? A good deal is heard about abuse of antibiotics. When should one prescribe penicillin or a tetracycline? When are the sulfonamides indicated vis-a-vis antibiotics?*

M.D., Pennsylvania.

Answer.—Opinion as to the best treatment of fever and infection of the upper part of the respiratory tract in a child of 10 years of age may well vary, depending on the physician queried. It also will vary according to the type of infecting organism and the severity of the illness. In general, it is a satisfactory practice to treat symptomatically for three days a child who has an infection of the respiratory tract. If at the end of that time improvement is taking place, the use of antibiotic agents is not indicated. If, however, there is no improvement or if matters become worse, antibiotic treatment should be instituted promptly. If the onset of the illness is severe, antibiotic treatment ought to be started at once. Knowledge of the clinical course of the same type of infection in other children in the community also is helpful in deciding the necessity for the use of antibiotic agents. If the infecting organism is a streptococcus, it is best to start treatment without a waiting period so that any complicating illness, such as rheumatic fever or nephritis, may be prevented. Penicillin, if the patient is not allergic to it, is the drug of choice for streptococcic infections, although tetracycline hydrochloride or a sulfonamide compound may be used. The drug should be administered for at least 10 days.

The choice of an antibiotic agent depends on the infecting organism and the patient's ability to tolerate the drug prescribed. Results of culture of specimens of nasopharyngeal secretions are helpful if bacteriological facilities are available. Strains of streptococci, staphylococci, Diplococcus pneumoniae, and Hemophilus influenzae are the organisms most commonly encountered. Viral infections are not treated by the use of antibiotic agents. If any antibiotic agent is used, it should be used for at least five days and sometimes longer, during which time it is administered in full therapeutic dose.

BRONCHITIS VACCINE

To the Editor:—*How efficacious is a stock vaccine for chronic bacterial bronchitis? What about autogenous vaccine? The patient does not have tuberculosis.*

M.D., Pennsylvania.

Answer.—At the present time, the use of either stock or autogenous vaccines seems to be regarded as of questionable value in the management of chronic bronchitis. For example, the use of such vaccines is not mentioned in articles on chronic bronchitis either in the "Principles of Internal Medicine," edited by Harrison and others (ed. 2, New York, McGraw-Hill Book Company, Inc., 1954), or in the "Textbook of Medicine," edited by Cecil and Loeb (ed. 9, Philadelphia, W. B. Saunders Company, 1956). In the section on acute bronchitis in the latter book, it is stated, "The use of preventive cold vaccines has, generally speaking, proved disappointing." The treatment of chronic bronchitis has been briefly reviewed by Lloyd (*Practitioner* 175:663, 1955), who states: "Many attempts have been made to treat bronchial infections by the use of so-called respiratory disinfectants . . . and by autogenous vaccines prepared from the sputum, but the results have been disappointing."

TOLERANCE TO ESTROGENS

To the Editor:—*What conditions in the mature female allow toleration of amounts of estrogens—naturally occurring or synthetic—far in excess of what can be administered with impunity to the average patient? The condition par excellence is the state of pregnancy, but are there any others? What about tumors? Is such tolerance dependent on proper liver function?*

R. J. Kent, M.D., Savannah, N. Y.

Answer.—Nausea and vomiting occur with all estrogenic substances, natural or synthetic, but are more frequent with stilbestrol, less with ethinyl estradiol, and least with such natural substances as conjugated estrone sulfate. That the nausea and vomiting is a central effect and not due to simple gastric irritation is borne out by its occurrence with parenteral as well as oral therapy. By far the most important organ in the intermediary metabolism of estrogens is the liver, where degradation to inactive substances as well as conjugation takes place. The marked intolerance to estrogens as well as the occurrence of skin "spiders" and gynecomastia in patients with liver disease attest to this fact. The tolerance of astronomic doses of estrogen by the pregnant woman is a well-established fact; its cause is not known, but it has been postulated as due to differences in metabolism in association with high levels of endogenous estrogen. On the other hand, it has been contended that the rising estrogen titer may account for the nausea and vomiting of early pregnancy, and the lack of side-effects to administered estrogen may be simply on the basis of increased tolerance due to this rise of the endogenous levels. Certainly, patients who do not tolerate large doses may well be able to take smaller and then gradually increasing doses with impunity. It must, therefore, be concluded that the patient can develop her own tolerance to the drug. Patients with estrogen-producing tumors of the ovary should be able to tolerate estrogens in high doses, but this cannot be definitely verified. This consultant knows of no tumor which specifically increases tolerance to estrogen therapy.

PLASMACYTOSIS

To the Editor:—*What is the clinical significance of plasma cells in the blood?*

M. L. Riccitelli, M.D., New Haven, Conn.

Answer.—Plasma cells (plasmacytes) are tissue cells which are extensively distributed particularly in those organs in which reticuloendothelial cells are abundant. The lymph glands, spleen, skin, bone marrow, and intestine are the normal sites in which plasmacytes reside. Plasmacytes may pass into the circulating blood in larger numbers in pathological conditions in which the total tissue plasmacyte mass is increased (see table). Except in infancy it is unusual to observe plasmacytes in the normal state in the circulating blood. The circulation serves as the normal transport pathway for the plasmacyte as well as other leukocytes, and an occasional plasmacyte may be observed in the blood without any pathological process being evident.

Significance of Plasma Cells in Blood

1. Not generally seen in normal blood beyond 1%
2. Non-neoplastic
    - Irritation of marrow
    - Hyperimmune states
        - Antigen-antibody reactions
        - Antibiotics and chemicals
    - Inflammatory conditions
        - Subacute bacterial endocarditis, granulomas (tuberculous, syphilitic, fungal);
        - asbestosis, silicosis, pneumoconiosis;
        - rubeola, rubella, varicella, scarlatina, infectious mononucleosis, infectious hepatitis;
        - *marrow regeneration, protein deprivation, starvation*
3. Neoplastic
    - Plasma cell leukemia
    - Plasma cell myeloma
        - Neoplastic invasion of marrow
    - Other leukemias

Plasmacytes (up to 60%) may be seen in the peripheral blood during severe immunological reactions or infections, e. g., serum sickness, rubella, rubeola, scarlet fever, chickenpox, infectious mononucleosis, or infectious hepatitis. Invasion of the bone marrow by metastases, particularly of epithelial origin, results in a plasmacytosis which may give rise to a secondary diagnosis of myeloma. Circulating plasmacytes may also be found in varying numbers in multiple myeloma and plasma cell leukemia. The increase is not necessarily a constant finding but is related to the size of the tissue plasma cell pool and the rate of delivery. During chronic inflammatory conditions, such as syphilis, tuberculosis, and chronic skin infections, an occasional transitional plasmacyte (Türk cell) may be found circulating. Plasmacytes may also circulate in infantile anemia with jaundice and during return from marrow hypoplasia from either chemical or radiation hematodepression and in states in which there is general hematopoietic stimulation.

BAN ON ORANGE COLORING

To the Editor:—*What is the toxic substance or substances used in coloring oranges? What are the effects on man? Is there enough toxic material from this source in marmalade to be injurious?* *M.D., Colorado.*

Answer.—The skin of oranges has been colored with a coal-tar dye called Red 32. However, since March 1, 1959, its use has not been permitted by the Food and Drug Administration because of possible carcinogenic effects; even though the skins of oranges are not usually ingested and no toxic effects have been shown in humans, it has been shown that Red 32 applied to the skin of mice will cause a cancerous growth. It is not felt that a sufficient amount of marmalade containing orange peels colored with Red 32 would be ingested to result in harm to the average consumer. However, in view of the prohibition, it is suggested that use of oranges on which this substance is known to have been applied be limited. Of course, this will soon no longer be a problem.

TREATMENT OF WARTS

To the Editor:—*Is there any treatment, except local destruction, for ordinary multiple warts? Please mention specifically the treatment for plantar warts.*

Joseph Sharpe, M.D., Farmington, N. Mex.

Answer.—There is only one type of wart that responds to anything other than local treatment, and that is the verruca plana juvenilis. Verruca plana juvenilis sometimes responds to such medication as low dosages of mercuric succinimide. The literature is replete with recommendations for innumerable types of local treatment of plantar warts. These methods include escharotics of various types, cryrotherapy, local injections, various forms of irradiation therapy, psychotherapy, and surgical intervention, including excision and even resection of the distal metatarsal head. In data on 1,300 cases, this consultant has found that by far the lowest percentage of recurrence is in patients in whom the verruca is removed by means of electrocautery. Local anesthetic is used. The entire growth must be completely removed by curettage down to the fatty layer, leaving a margin of normal skin about the wound. When all of the verruca has been removed by curet and repeated cauterization, the remaining normal tissue, both the walls, and the base of the wound are desiccated and a dressing applied with an antiseptic ointment. The dressing is changed every several days until epithelization has taken place. If the destruction has been wide and deep, it may produce a painful site. Discomfort may be alleviated by relieving pressure on the wound. This is accomplished by cutting an opening the size of the wound in a small square of foam rubber, ¼-¾ in. thick, and applying this with adhesive over the outer surface of the dressing. The wound ordinarily heals in about 10 days to two weeks. With proper management the patient should not be incapacitated.

ENDOMETRIOSIS

To the Editor:—*Is there any scientific basis to the common saying that the woman with endometriosis should omit milk from her diet? A 43-year-old nulliparous woman with endometriosis was operated on several years ago and one ovary removed (chocolate cyst). Recently she was operated on again, and widespread endometrial tissue was found, only a fraction of which could be removed; the uterus was left intact because it was adherent to the rectum, but the second ovary was cystic and was removed. Please outline the postoperative management for hormonal (estrogen) replacement. Does it differ from that after any other oophorectomy? The menstrual history had been normal, except for dysmenorrhea.*

Calvin P. Wallis, M.D., Norman, Okla.

Answer.—This consultant knows of no basis, scientific or otherwise, for depriving women who have endometriosis of milk. This patient reported may have no symptoms of the menopause. Because of extensive earlier endometrial involvement of the ovaries, ovarian function probably was decreasing over a period of years. If this patient is disturbed by severe hot flushes or other symptoms that can be definitely attributed to the menopause, then estrogen therapy may be indicated. Small doses of stilbestrol, 0.5 mg. at bedtime, may be adequate. This is usually not enough to cause bleeding unless it is suddenly withdrawn. After the symptoms have been relieved, the dosage should be gradually decreased. If the small dosage is not adequate to relieve the symptoms, the dose of stilbestrol should be gradually increased to 100 mg. daily. This can be done by starting with 0.5-mg. tablets and increasing the dose by one tablet every third night until the equivalent of 6 mg. is taken every night. Then one-fourth of a 25-mg. tablet may be given and the dose increased one-half tablet every third day until the patient is taking 100 mg. daily. This dosage is continued for three months; then the drug is gradually withdrawn over a period of a week.

YELLOWING OF HAIR

TO THE EDITOR:—*A woman in her early 50's whose hair had previously become completely white is developing increasing yellowness of the hair. The patient uses a well-known commercial shampoo only. She has received at various times recently the following medicaments: atropine methylnitrate, 1 mg., with phenobarbital, ¼ grain (15 mg.); danthron, 75 mg. (⅓ tablet) occasionally, not daily; piperidolate hydrochloride, 50 mg.; chloroquine phosphate, 250 mg. once daily; prochlorperazine, 5 or 10 mg.; glutethimide, 0.5 Gm.; methyprylon, 200 mg.; multiple vitamins; dioctyl sodium sulfosuccinate; ethinyl estradiol, 0.05 mg. once or twice daily; and thyroid. Might any of these drugs be related to yellowing of the hair? Please suggest a remedy.*

Robert A. Straughn, M.D., Madison, Wis.

ANSWER.—A change of hair color may occur as a result of any one of several factors. In this particular instance, the only external contact involved is apparently with the shampoo mentioned and this could not produce the color change. Of the internal medicaments listed, this consultant would immediately withdraw the chloroquine, inasmuch as there have been several reports of discoloration and change in hair color after ingestion of antimalarial drugs. With this therapy discontinued, the probability exists that the hair will return to normal after an adequate period of time to permit elimination of the drug from the body. It would not be necessary to withdraw any of the other medicaments, which are presumably necessary for her medical condition, until effects of discontinuance of therapy with the antimalarial agent have been observed.

CHEST TRAUMA AND CORONARY ATTACK

TO THE EDITOR:—*Is there any causal relationship between trauma of the chest (especially over the heart area) and the precipitation of an acute coronary occlusion with infarction in a patient with existing coronary arteriosclerosis? If so, what period of time usually elapses between the trauma and the infarction?*

M.D., Florida.

ANSWER.—Trauma of the chest wall must be of considerable extent, as a rule, to cause any injury to the heart. The commonest injury, 96.8% according to Bright and Beck (*Am. Heart J.* **10**:293, 1935), is cardiac rupture. Contusion of the heart requires a degree of violence sufficient to fracture the bones and cartilages of the chest wall and to cause severe traumatic injuries to the thoracic viscera. The experience of the Medical Examiners Office in New York City, reported in the book "Legal Medicine: Pathology and Toxicology," by Gonzales and others (New York, Appleton-Century-Crofts, Inc., 1954), would indicate that a causal relationship between trauma of the chest and the precipitation of acute coronary occlusion with infarction in any patient, whether there is preexisting coronary arteriosclerosis or not, is rare. The authors know of only one such case. There was severe chest injury as well, resulting in rapid death from hemorrhage and shock. Articles in which cases are reported of presumable relationship between chest injury and coronary thrombosis are usually unsupported by careful autopsy data. Injuries of the coronary arteries due to nonpenetrating blunt force are exceedingly rare and do not occur in an isolated form. In rare cases when they do occur, there are always substantial and easily demonstrable injuries to the chest wall and contents and to other parts of the heart and great vessels.

BREAST CANCER AND ESTROGENS

TO THE EDITOR:—*A 50-year-old woman had a radical mastectomy for carcinoma of the breast seven years ago and has been symptom-free since then. Menses ceased completely about one year ago. Hot flashes are still present, and no specific treatment has been given for these. Recently, involutional vaginal changes with dyspareunia have developed. Could daily application of 2 to 4 Gm. of an estrogenic vaginal cream (containing 1.25-2.5 mg. of conjugated estrogenic substances) result in sufficient absorption to be contraindicated in view of the history of mammary cancer? If not, for what length of time may applications be continued?*

M.D., Illinois.

ANSWER.—Seven years is insufficient time to be certain that the breast malignancy has actually been cured. It is better to rely on 10 years, but this is not always a final time. Any of the estrogenic preparations, whether natural or synthetic, might have undesirable influences on any breast malignant cells still present in the body. This is a view commonly accepted today. It is one reason why some surgeons feel strongly about removal of the ovaries prior to the menopause in women with mammary malignancy. Although there is a possibility that estrogen might not have a deleterious influence, it would seem that a patient of this age should have other methods of treatment for the vaginal condition. There seems to be ample evidence that estrogens are absorbed through the vaginal mucosa. If one could be assured this patient was totally cured, estrogens could be used, but a state of doubt does exist. In this particular instance, it is best to avoid use of estrogens at this time.

WASHINGTON NEWS

Congressional Hearings on Forand Bill . .
A. M. A. Testimony . .
State Societies Review Progress . .

HEARINGS ON FORAND BILL

The House Ways and Means Committee heard more than 50 witnesses, during five days of hearings, argue for and against the controversial Forand bill to provide hospital, surgical, and nursing-home treatment to some 16 million persons through the Social Security system.

At the conclusion of the sessions, July 17, there was no indication whether the committee, headed by Rep. Wilbur Mills (D., Ark.), would take a vote on the legislation. Last year hearings also were held, but no action was taken on the measure sponsored by Rep. Aime Forand (D., R. I.), second-ranking Democrat on the committee.

The administration came out flatly against the measure. Arthur S. Flemming, Secretary of Health, Education, and Welfare, said it would be "very unwise" for Congress to approve the legislation.

Flemming asserted that the measure would establish a course from which there would be no turning back—that health coverage of the aged would "become frozen in a vast and uniform governmental system, foreclosing future opportunity for private groups, nonprofit and commercial, to demonstrate their capacity to deal with the problem."

He said that as far as possible the aged should be provided with medical care through voluntary individual and organized action. He pointed out that private health insurance has increased rapidly in recent years and predicted that 70% of the aged will have some form of health insurance by 1965.

There is no question but that the legislation "would bring to a virtual halt the voluntary efforts that are moving forward in such an encouraging manner," said the administration official. He warned that a Forand-type program would result in strong pressures to extend the benefits further, with the result that voluntary insurance "might soon be eliminated from the entire field of health protection for the aged."

Representative Forand, who questioned Flemming at length, asked why private insurance could not supplement a federal program, rather than be eliminated by it. Flemming said that the Forand program provides "reasonably adequate services" and that people would not be likely to duplicate coverage out of their own pockets.

Spokesmen for the American Medical Association and 33 state medical societies joined in urging the House committee to turn down the measure.

The American Hospital Association strongly opposed the legislation, with a spokesman contending that "the government as a purchaser of so much hospital care would exert the power of the purse in ways detrimental to the interests of hospital patients."

The AFL-CIO renewed its backing of the measure. An official of the labor organization told the committee that private insurance will never be able to handle the task of financing medical care for the elderly. Other proponents included the Physicians Forum, the National Farmers Union, the National Association of Social Workers, the American Public Welfare Association, Americans for Democratic Action, and the United Auto Workers.

Organizations that supported the stand of the administration, the A. M. A., and the AHA included the American Farm Bureau Federation, the Chamber of Commerce of the United States, the American Society of Internal Medicine, the American Dental Association, the American Pharmaceutical Association, the National Association of Manufacturers, the Life Insurance Association of America, and the Health Insurance Association of America.

Dr. R. B. Robins, a member of the A. M. A. Board of Trustees, speaking for the American Academy of General Practice opposed the measure and said it might lead to conditions such as he viewed on a recent trip to Great Britain to inspect the socialized medicine system.

A. M. A. WITNESSES

Officials of the American Medical Association and 33 state medical societies outlined to the House Ways and Means Committee the medical profession's contention that enactment of the Forand measure would stifle progress being made voluntarily, and hurt rather than help the quality of health care for the aged.

Dr. Frederick C. Swartz, Chairman of the A. M. A. Committee on Aging, and Dr. Leonard Larson, Chairman of the A. M. A. Board of Trustees, stressed the rapid progress in private health insurance and the dangers of a government health program. Representatives of the societies pointed to widespread advances in state programs.

Dr. Swartz testified that medical care is not susceptible to production-line techniques. A cooperative attack by all professions involved, including the medical profession, is needed, he said. Flexibility would vanish "the moment government established a health program from a blueprint calling for mass treatment," the witness declared.

Dr. Larson said he was proud to inform the committee that the A. M. A. is making good on the pledge that it gave the lawmakers a year ago to a dedicated continuing effort in the field of health care for the aged. "Very real progress" is being made, he said, with [illegible] villages, new nursing homes, chronic disease–care

(Continued on next page)

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Lown, B., and Levine, S. A.: Current Concepts in Digitalis Therapy, Boston, Little, Brown & Company, 1954, p. 23, par. 2.

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centers, home-care programs, and other projects. "And many, many more are on the way," Dr. Larson said.

Asserting that the legislation is "neither practical nor realistic" Dr. Swartz listed as some of his reasons that it would curb community incentive to support hospitals, discourage at the community level the freedom to experiment with new techniques, discourage families from taking care of their relatives, restrict beneficiaries in their choice of hospital and physician, and severely handicap the professional relationship between the doctor and his patient.

In addition, said Dr. Swartz, the program would be staggeringly expensive, costing more than 2 billion dollars a year. The measure, he contended, "simply proposes a form of national compulsory health insurance."

Summing up his statement Dr. Larson told the committee that "a compulsory system can lead only to disillusionment and to inferior medical care for those millions of older citizens who deserve the opportunity of making their extra years rewarding."

STATES REPORT PROGRESS IN AIDING ELDERLY PERSONS

Spokesmen for state medical societies presented a united front in opposition to the Forand bill. They told the Ways and Means Committee of substantial strides in their states to meet the problems of medical care for the aged. Testimony or statements were presented by representatives of 33 state societies.

"There is every reason to believe that it is still the problem of the individual, his family, the community, religious groups, and local political subdivisions, working with the various purveyors of insurance coverage to solve it—in the American way," testified Dr. Carl Fortune of Lexington, Ky., president-elect of the Kentucky Internal Medicine Society.

Dr. Daniel H. Bee of Indiana, Pa., representing the Medical Society of the State of Pennsylvania, asserted that "organized medicine and other interested groups have [worked] and will continue to work with these problems until they are solved in our state."

Another witness, Dr. Joe Johnson, speaker of the house of delegates of the Tennessee State Medical Association, said passage of the Forand bill would undermine the far-reaching and substantial progress now being attained by voluntary methods in Tennessee through health insurance.

The Texas Medical Association reported that it "is fully engaged in a multiphased program which is designed to alleviate many existing problems related to medical and surgical services for the aged." Speaking for the society was Dr. Milford O. Rouse, former president of the Texas Medical Association.

Dr. John R. Kernodle, chairman of the North Carolina Medical Society's committee on chronic illness, testified that North Carolina has pioneered in home-care and homemaker service programs for rural areas and that the voluntary approach to meeting the health problems of the aged is getting results in his state.

Dr. T. Eric Reynolds, president of the California Medical Association, said compulsory national health insurance would "destroy many helpful voluntary programs" that are proving of real benefit to California citizens aged 65 and older.

The position of the Iowa physicians was presented by Dr. Noble W. Irving of Des Moines, chairman of the state medical society's committee on legislation. "Iowa physicians have reached a degree of unanimity seldom attained in, first, proposing and carrying out a positive plan of action for improving voluntary ways and means of financing health care for our senior citizens, and, second, in opposing this proposed legislation."

"In Florida, no one who needs it goes without hospital care," said Dr. H. Phillip Hampton, chairman of the committee on legislation and public policy of the Florida Medical Association. "This includes those over 65 years of age."

Dr. George E. Twente, representing the Mississippi State Medical Association, told the committee that "our voluntary prepayment plan, the Mississippi Hospital and Medical Service, was one of the first to develop a Blue Shield-Blue Cross package contract geared to health needs of senior citizens. Growth of medical and related facilities in Mississippi since 1946 has been astonishing."

Dr. Renaio J. Azzari, member of the Board of Trustees of the Medical Society of the State of New York said, "There is no need for federal intervention, through this bill, in New York state. State and local governments have done an excellent job in providing for the aged." Of the population of the state 88 percent are now covered by some form of hospital insurance, and "it can be expected that greater advancements will take place in the future."

Dr. Vincent W. Archer of the Medical Society of Virginia testified that a special insurance policy related to the maximum income of Social Security recipients is under serious consideration in the state. "We are convinced that as programs of this nature become more widespread the competition of the marketplace for the ever-growing number of the aged can only result in better and better coverage for this group."

MISCELLANY

The Senate Finance Committee held a final one-day hearing on the Keogh measure to encourage the self-employed to invest in retirement plans. Its purpose was to allow spokesmen for organizations favoring the legislation to present their testimony, since there was not enough time at sessions earlier this year. Backing the House-passed bill at the hearing were officials of the American Optometric Association, the American Veterinary Association, the National Small Businessmen's Association, the American Retail Federation, the Chicago Bar Association, and the National Council of Salesmen's Organizations. Another day of testimony was planned later this session.

The Senate approved $88,800,000 for the Defense Department's Medicare program for the current fiscal year, the same figure cleared by the House. The Medicare program was part of an over-all 40-billion-dollar defense money measure.

The Senate completed congressional action on an administration-approved bill to extend for five years current programs of federal aid for advanced training in public health and professional nursing. Proposals by some lawmakers to broaden the program that were opposed by the administration were not included in the measure.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June 13-17.

AMERICAN

1959

July

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semi-annual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Mississippi Valley Medical Society, Hotel Chase, St. Louis, Sept. 29-Oct. 1. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Ill., Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. Mr. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executive Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 28-Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, The Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeons, Chicago, Sept. 13-17. For information write the Secretariat, 1516 Lake Shore Dr., Chicago 10.

Ohio Society of Anesthesiologists, Dayton Biltmore Hotel, Dayton, Sept. 18-19. Dr. Nicholas G. DePiero, 9710 Garfield Blvd., Garfield Hts. 25, Ohio, Secretary.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-25. Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executive Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-29. Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Chairman.

United States Section, International College of Surgeons, Palmer House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Shore Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt Lake City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City 2, Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Sept. 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cleveland, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, The Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, Oct. 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hotel, Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Room 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hotel, Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St., Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Philadelphia, Oct. 23-25. Dr. Philip Reichert, Empire State Bldg., New York 1, Executive Director.

American College of Chest Physicians, 25th Anniversary Homecoming Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, Atlantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philadelphia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New York 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, Oct. 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conrad Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic City, N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic City, N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, Bal Harbour, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St., Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Hotel Fontainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray Broadbent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Hotel, Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road, Miami 33, Fla., Executive Secretary.

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PRACTICAL STEPS FOR THE FAMILY PHYSICIAN IN THE PREVENTION OF EMOTIONAL DISORDER

Gerald Caplan, M.D., D.P.M., Boston

The style of work of the family physician is fundamentally different from that of the psychiatrist, but the family physician who seriously wishes to enlarge the scope of his practical operations with respect to the mental health needs of his patients does well to build up a working relationship with a psychiatrist of his choice. This can greatly improve his ability to recognize emotional needs in families, to prepare married couples for emotional problems like those of pregnancy, to help families go normally through periods of separation or bereavement, and generally to use his knowledge of the family in order to contribute to its stability. His traditional role brings him into contact with many people at times of crisis. At such times he can exert a particularly powerful effect on their mental health by steering them away from maladaptive solutions and toward adequate solutions of their life problems.

THE etiology of emotional disorder in any individual case is very complicated. Many interacting factors are involved, including those based on constitution, childhood experiences, later life problems and their solution, and details of the unfolding of the processes of growth and development in interaction with the forces of the emotional and material environment.

If one looks at this problem from an epidemiologic point of view it is still complicated, but it is simpler: by this I mean a study of the factors in one community which are responsible for its having a higher incidence of cases of emotional disorder than another community. Such studies isolate certain common factors which operate to influence all members of a community. These factors do not determine the fate in any individual case, but they lead to communitywide differences in the frequency of certain psychological illnesses.

Viewed from this standpoint it is possible to discover certain general factors which can be combated on a communitywide level. Programs to alter these factors may not affect the fate of any particular person but are likely to reduce the number of cases which occur during a subsequent period in that community.

In connection with these factors the following consideration seems important: The mental health of an individual is dependent on the continuous satisfaction of special requisites in the patterns of his psychological interaction with certain other people. We can speak loosely about a person having psychological needs which have to be satisfied in his interactions with others. The most obvious need

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Associate Professor of Mental Health, Harvard School of Public Health.

Based on a lecture read before the Honolulu Medical Society, August, 1957.

is the basic psychological stimulation of having people to talk to. For years we have realized that isolation has a potent harmful effect on mental health. For centuries men have tortured their fellows by marooning them on desert islands, by solitary confinement in prisons, or by ostracism in the social setting. The list of needs also includes the opportunity to give and receive love and affection, to be dependent and to be depended on, to satisfy cravings to be controlled and to control, and to be a member of a social group in which one's identity and personality are respected and accepted, so that one's achievements are rewarded by praise and one's difficulties are lightened by sympathy and understanding.

In all cultures there exist within the structure of the society small groups of people who are bound together by significant emotional ties, and within these groups the psychological needs of the individual members are satisfied. Biological ties are usually the basis of these fundamental groupings, and some form of family structure is universal. In different cultures the pattern of families varies, but, whether one studies the small family of modern Western urban culture, the large extended family of earlier Western rural culture or certain present-day Oriental cultures, or the matriarchal families of other cultures, we find that certain roles or tasks of psychological significance are allotted by tradition to each of the family members, that the sum of these tasks usually satisfies the needs of all the members, and that this sum is distributed among the members of the group so that no necessary role is left out.

In recent years we have discovered that the interactive possibilities afforded by the intact structure of the family are as necessary to mental health as the provision of adequate nutritional supplies are to physical health. When the traditional pattern of any family is altered by situational factors, the mental health of its members is endangered. This danger is greatest for the younger children, in the same way that nutritional deficiencies are most dangerous during early developmental phases, but the danger is also present for the mature adults.

Another similarity to physical nutrition is that if all goes well we do not usually realize the importance of these factors. The satisfaction of needs in an intact family takes place silently and automatically. It is only when the family structure is deficient that difficulties become obvious; since families are ubiquitous it has taken us a long time to realize the obvious fact of their importance for mental health and the close connection between defects in their structure and subsequent emotional disorders among certain of their members.

Importance of the Family Physician in Promoting Mental Health

From all this it follows that professional workers who deal with people as members of a family have a special place in programs of mental health promotion. The family physician is a worker with a uniquely important role in this regard. He is usually called in to a family to handle symptoms of physical disorder in one or more of its members. In dealing with this traditional task he may well add another dimension to his practice and focus his interest on those elements of the situation which involve dangers to the social structure of the family group, therefore involving dangers to the future mental health of its members. The concept of the family as a unit, and the physician as a worker with responsibilities to the whole unit, implies not only that he may accept as a patient any individual family member but also that when he is called in to deal with the symptoms of one member he will widen the focus of his interest to include all the others, whether from the point of view of their involvement in the etiology of his patient's condition or from the point of view of the effects of his patient on them as a group. This responsibility has been clear for years in cases of contagious disease, but we now realize that it applies equally, if not more so, to the social and psychological side-effects and sequelae of any illness. This latest insight is, as is often the case in medicine, a reformulation of old traditional knowledge; the family physicians in our parents' generation understood this quite well, although they may not have been able to spell it out as explicitly as we can nowadays. Increasing complexity in the medical sciences, increasing specialization, and increasing concentration on the exciting new discoveries in somatic medicine have to some extent pushed these old insights into the back of our minds. In the hurly-burly of busy practices, and in the absence of strong protagonists, they have fallen into disuse.

Moreover, the older training of physicians by the apprentice system allowed young men to acquire many of the skills of psychosocial management of the family by modeling themselves on the practice of experienced preceptors. The knowledge they acquired was not to be found in books but in the life situations of their apprenticeship. Nowadays the old type of apprenticeship is usually missing, and the books still say very little about all this—at least very little that is useful at a practical level—because the writers of these books have usually not carried out their studies within the framework of the actual situations of general medical practice but in the very specialized and unique conditions of psychiatric clinics and psychological laboratories.

Exhortations by psychiatrists that the family physician should play his part in promoting mental health are no great help. The family physician asks, "Exactly how should I do this?" and the psychiatrist usually has no concrete answer. In this paper I will attempt to begin to give a concrete answer—or at least to indicate specific avenues for practical exploration.

Before ending this introduction, I would like to mention one other point which supports the importance of the family physician in community programs of preventive psychiatry. He is one of the key community workers who has contact with people when they are in a state of crisis. Physical illness may be a turning point which determines a change in the whole course of a person's existence; it is important to realize that during the relatively short period of the few weeks or months of the illness all kinds of decisions may be made and all kinds of psychological reorientations, as well as alterations in the structure and functioning of families, may be worked out which will affect the type of interpersonal relationships and character of intrapersonal functioning for a long time to come.

Psychiatrists have recently joined the ranks of those who are very interested in the way people solve the emotional and social problems of periods of life crisis. Previously, it was mainly novelists and dramatists who were interested in this topic, but nowadays we psychiatrists realize that the future mental health of people may be determined at crisis times by the quality of their problem-solving methods. One type of solution of a set of problems may lead to greater mental health, which explains why many people become more mature as a result of satisfactorily overcoming life's difficulties. Another type of solution may lead to mental ill health, either immediately or in the future, and either directly for that individual or indirectly for his dependents due to damage of his emotional relationships with them.

People become emotionally disturbed during these crisis periods, but the anxiety, depression, tension, and hostility are not to be confused with symptoms of psychiatric illness, which they superficially resemble. They are the signs in the emotional sphere which show that an active struggle is in process inside that individual in his attempts to wrestle with his problems. At the end of the few weeks of crisis these symptoms will disappear, once some kind of solution has been achieved. This solution may be a healthy one. On the other hand it may be an unhealthy one, and in that case either at once or in the future the individual will manifest neurotic or psychotic symptoms which represent a pathological way of dealing with his life problems through some form of irrational and psychologically distorted pseudo-solution.

The most important point for preventive psychiatry is that the type of problem solving during a crisis can be powerfully influenced by the helpful or hindering intervention of other people, both in the family circle and from the outside, in the form of the physician and other community agents. When the balance of forces is upset in a crisis a minimal intervention may produce major and stable results by determining to which side the balance will come down.

This means that the operations of the family physician during any of his visits for whatever reason to a family in crisis may have a major effect on the pattern of resolution of that crisis and on the members' future mental health.

I wish now to concentrate on examples of certain practical implications for the operations of the family physician that arise out of these theoretical considerations.

Safeguarding the Integrity of Family Structure

The general practitioner has many opportunities in his practice to help keep families from breaking up temporarily or permanently; or, if this can not be avoided, to help them find substitutes for roles which the family break-up has left vacant.

Most important is the prevention of separation of the mother from the family circle or from one of her children. Bowlby[1] and other workers have shown fairly conclusively that the separation, for any appreciable time, of the stable mother figure from a child during the first few years of its life exerts a damaging effect on the development of the child's personality, leading in severe cases to extreme forms of psychological and psychosomatic illness. If the physician is aware of this, he will be alert to explore practical alternatives to any plan for removing a mother or a child from the home because of illness. Often the removal from home is quite inevitable because the nature of the illness demands hospitalization, but frequently the physician may be able to plan for this absence to be short and for the remainder of the treatment to be carried out at home. The fact that the mother is physically incapacitated certainly will influence her ability to fulfill many of the demands of the mother role, but her mere presence in the home will allow her, through repeated contacts with other family members, to maintain the emotional bonds of comfort and sympathy and mother love which are the emotional nutrients the others need.

Of course such a plan implies the need for nursing and homemaker services to care for the patient at home and to take over her housewifely duties. The physician should be active in helping the family secure such services either from the ranks of the extended family of grandparents, aunts, sisters, and cousins; from neighbors and friends; or, if these are not available, from professional workers. When the latter are not available I believe that local physicians should actively campaign among appropriate community agencies for their provision. Family physicians should be as interested in the adequacy of community agency provision in this area of homemaker services as they are in the standards of their local hospitals, since both affect the quality of the professional care they can give their patients.

The feeling in regard to hospitalization of young children should be that of avoiding or postponing or shortening it whenever possible. With modern methods of diagnosis and treatment and effective home nursing, many types of cases which in the past necessitated admission to children's hospitals can be treated at home.

When separation is inevitable the physician should encourage frequent and regular visiting to maintain channels of communication and continuation of the emotional links.

In 1952 in England, as a result of Bowlby's researches, the Ministry of Health issued a directive to permit and encourage daily visiting in children's wards. In the United States this is also becoming common pediatric practice, and some new children's hospitals have facilities for parents to sleep in the ward near their child and help with certain nursing procedures. This has led to inevitable complications in ward management and new problems for the nursing staff, but none of these have proved insoluble and they are a small price to pay for the results in terms of the safeguarding of the personality development of the children.

The physician interested in the whole family should also be on the alert for the neglect of the other children when one child is hospitalized. He should try to mobilize the efforts of other family members to cover the hiatus left when a mother is concentrating her efforts on the ill child, and his activity in this regard should not stop when the ill child comes home. We are familiar with many cases of neurotic disturbance in children which started during periods of parental neglect due to the illness of a sibling.

If the mother has to go into the hospital, the physician should try to promote communication from her to the other family members, particularly the children, through frequent verbal and written personal messages; he should also use his best efforts to help the rest of the family stay together in their home. If the family stays together they may close their ranks and take over, as a group, some of the absent member's functions, whereas if they are split up this group strength is dissipated.

In order to keep the family together the physician may have to mobilize other family members to come in and do the housekeeping, or he may have to call in a homemaker. Placing the children as individuals in other homes may seem the easier way, but it is actually more expensive in both the short run and the long run.

Another area where the family doctor can give invaluable mental health help is that of helping the father take over some of the maternal role left vacant by the absence of his wife. Husbands may need support and explicit encouragement and advice in mothering their children during this period and in assuming unaccustomed leadership in housekeeping. Some men may be rather inhibited in doing what is needed because of false feelings of shame about such activities being effeminate. The physician can watch out for this and throw the power of his prestige behind the medical prescriptions to the hesitant father.

When the separation of the mother is permanent due to death or desertion the physician should interest himself actively in helping the family plan for her replacement by a substitute. Assistance in this direction, as in the other issues which have been mentioned, may be obtained from a family social agency; but the family physician, who is the professional person with continuing contact and responsibility for the whole family, should help in mobilizing this assistance and should coordinate these activities with his own and with those of other helping agents such as clergymen and teachers.

The physician should be equally active if it is the father and not the mother who is separated from the family by illness, death, or social factors, such as employment demands or wartime needs. A wife needs her husband's support, and children need the controlling influence of a father figure. This issue has been relatively neglected until recently. Interest in it has now been aroused by the realization that many common disorders of personality development in children, which lead to delinquency, have been influenced by the absence of a stable controlling father during the child's upbringing, so that the external discipline which is the precursor of the internal discipline of the socialized person has been missing or defective.

If there is no man in the house, the role of discipliner of the children devolves largely on the mother, and she may need the support of the physician, himself a potent father figure, in order to add this to her other roles. It may also be possible for him to help her out directly in certain crisis situations and to invoke the help of teachers and recreational group leaders.

Perhaps by now it seems that I am advocating turning the general practitioner into a social worker. Nothing is further from my intention. His primary role must remain that of the practitioner of the healing arts; but if our talk of treating the whole person rather than the diseased organ is to be more than a mere slogan, we must expect the physician to add an interest in some of the above psychosocial points to his traditional preoccupation with physical functioning. The family physician may well realize that his role in the family provides him with both the responsibility and the opportunity to affect its functioning in ways which will have direct effects on the health of its members. So long as mental health and mental illness were conceived of as being quite separate from physical health and physical illness, the physician could afford to neglect some of these issues; but nowadays such a dichotomy is hard for most of us to accept and very hard indeed for the general practitioner who deals not with bits of people or special aspects of their functioning, as isolated in special clinics, but with the whole fabric of life within the family circle in the home.

Safeguarding Healthy Relationships

The satisfaction of individual psychological needs in the family is dependent not only on the preservation of the integrity of its structure but also on the quality of the enduring interpersonal relationships among its members. The mother may not be geographically separated from her child, for example, but her prevailing feelings toward him may be so anxious, ambivalent, or rejecting that she cannot perceive his needs, or, if she does, she may have no interest in satisfying them.

Once disordered relationships between family members have fully developed, treatment by a psychiatric specialist is usually needed to improve them; unless such intervention is forthcoming, a significant proportion of the people will eventually need psychotherapy for manifest psychiatric illness. In the past few years, however, we have discovered that the disordered relationships which are harmful take quite a time to develop to their full pathogenic intensity and that during this period the family physician may interrupt this harmful development. His helpful intervention can best be focused at certain crucial periods when disorders in relationships are most apt to occur in response to characteristic temporary situational factors.

Pregnancy.—One such crucial period, both for the development of the mother-child relationship and for the other interpersonal relationships in the family, is the period of pregnancy. The mother's relationship with her new baby does not begin at his birth but is being built up during her pregnancy; the complicated metabolic development of this period has a characteristic effect on her emotional functioning, which in turn has reverberations on the emotional life of the family as a whole. These reverberations may lead to changes in the way the family members relate to the expectant mother and to each other, and these changes may become stable and may have far-reaching consequences for mental health by altering the pattern of need satisfaction within the family circle.

Recent studies [2] on the emotional manifestations of normal pregnancy have yielded information about characteristic series of emotional changes which occur in many expectant mothers and which are apt to frighten them and to interfere with family life. The physician who knows the details of this predictable development may make powerful use of this knowledge.

His main technique will be anticipatory guidance, whereby he warns the patient and her husband ahead of time what to expect and thus gives them the chance of preparing themselves psychologically for the difficulties. For instance, quite early in pregnancy the physician should have a joint interview with husband and wife and let them both know that many women become more irritable and more sensitive than usual during pregnancy because of complicated and little-understood somatopsychic factors; therefore, if in this case the expectant mother suddenly gets angry with minor provocation, laughs or weeps for no adequate reason, or has sudden attacks of depression, neither she nor her husband need get alarmed. These changes, however dramatic, are not preliminary signs of psychiatric illness and they will disappear after delivery.

At this early conference the physician will also be well advised to mention the likelihood of changes in the pregnant woman's sexual desire and performance. Changes in appetite are frequent in pregnancy, and this relates not only to foods but to sex. In regard to this topic the physician not only gives needed anticipatory guidance but often is able to act as a channel of communication between husband and wife in relation to topics which in our culture may not be easily discussed between them. In the absence of necessary knowledge and in the presence of communication blocks so that difficulties cannot be worked out by discussion, tensions may easily arise between husband and wife based on distorted interpretations of each other's attitudes. A wife, not infrequently, gets very upset if she loses her sexual desire or capacity for orgasm; she imagines she has become permanently frigid or that she is losing her love for her husband and that he will reciprocate in kind. A husband sometimes fears that his wife is rejecting him because he made her pregnant, and sometimes he seeks alternative sources of sexual satisfaction as a reaction to this imagined rejection. Such unfortunate fantasies can be easily alleviated by the physician's prior discussion of the realities of the situation. He can also help both parties become aware of the strain under which each will be laboring during pregnancy and help them pay special attention to the need to support and sympathize with the partner's difficulties and to make allowances for signs of tension.

Such joint interviews with husband and wife, which should if possible be repeated at least once or twice more during the pregnancy, have a more essential function than just the smoothing out of expected difficulties in the marital relationship, important as this is. My studies have shown that toward the middle of pregnancy most women become more passive and demanding of affection than usual. Instead of being the giving person in the home, actively attending to the needs of others, they now turn in on themselves and feel the need to sit around and be waited on. My studies have also shown that the adequate satisfaction of these needs for increased attention and affection is not only important for increasing the expectant mother's comfort but also plays an important part in preparing her for adequate motherhood in the first few months after delivery. If she receives enough affection during pregnancy, she can give out enough affection to the baby. Those women who are deprived during pregnancy later have a tendency to deprive their babies.

Recognition of this by the physician allows him to play an important role in ensuring adequate emotional supplies at the crucial early period of the newborn infant's life. He cannot give the expectant mother affection himself, but he can try to make sure she gets it from the natural sources. There are many cultural and psychological factors which may block a husband's demonstrations of affection during pregnancy. He may be so irritated by his wife's petulant behavior and by her inability to afford him his usual sexual satisfaction that he turns away from her. He may be frightened by her increased demands, and he may feel she is changing her personality and becoming lazy and spoiled. He may resent what he feels is her exploitation of the privileges of pregnancy. His feelings of security in his manly role, which are in our culture often weakened by the lack of respect we pay to expectant fathers, may be further endangered by his wife's demands that he take over some of her maternal functions in the work in the house or caring for the other children.

The physician has the opportunity during his joint conferences with husband and wife, or if necessary during an individual interview with the husband, to prevent the difficulties which may emerge from these factors. He can reassure the husband as to the normality of his wife's reactions and as to their temporary nature, and he can enlist the husband's active help in preparing for the baby by, as it were, "charging up his wife's battery of affection," so that she can eventually pass the emotional supplies on to the baby. Most important, the physician can by his own attitudes during these meetings help increase the husband's feeling of respect for the importance of his own role as an expectant father. This may help to prevent a not infrequent cause of family difficulty after the baby arrives, when some fathers are hampered in their paternal role by feelings of jealousy in regard to the baby.

I do not wish to leave this very brief reference to the physician's preventive role in emotional disorders originating during pregnancy without mentioning the results of some recent research which has specific practical implications. My studies have shown that certain traumatic events occurring during the period of pregnancy exert a powerful harmful effect on the future mother-child relationship. Such events include the severe illness or death of a near relative of the expectant mother, particularly of a parent, her husband, or one of her children. It is very easy for the woman to displace some of her painful feelings about such an event onto her relationship with her unborn child, and her attitudes toward him get distorted by irrational ideas, such as identifying him as a reborn representative of the dead person or blaming him and sacrificing him because of unresolved feelings of personal guilt in connection with the bereavement. The physician should be especially on guard to ensure an adequate process of mourning along lines I will describe below, and he should help the mother to see and to feel that her new baby is an individual in his own right and has to be recognized and treated as a person with quite a separate fate from everyone else, including the dead person.

Abortion.—Another traumatic event during pregnancy which is likely to have a major harmful effect on the future mother-child relationship is an attempt by the mother to abort herself, if this act is against the rules of her culture and traditions, and especially if she keeps it as a guilty secret. It is this guilt which blossoms in secret fantasies and which invades and distorts the relationship with the child. If nothing is done about it, the chances are high that a particularly pernicious disorder of the child's personality will eventually be produced. The important point is that this pathological sequence of events can usually be easily interrupted by the family physician, if he identifies either during pregnancy or soon afterward what has happened. The technique to be used is one which is not usually a part of the general practitioner's therapeutic armamentarium but one which can be fairly easily learned, namely, specific reduction of conscious guilt. I have discussed this at some length in a recent paper,[3] and here I will only mention it briefly. It consists essentially of the physician helping the woman to talk about what she has done in two to three short interviews, in which he adopts an understanding and nonjudgmental attitude toward her behavior, without in any way pretending that what she did was a good thing and yet with the clear demonstration that despite what she has done he continues to accept her as a worthwhile person.

Direct Help to People in Crisis

The traditional role of the physician brings him into contact with many people during the critical period when they are wrestling with acute life problems, and at such times he can exert a particularly powerful effect on their mental health by steering them toward adequate solutions and away from maladaptive solutions. The clearest example of this is in connection with problems of bereavement.

Bereavement.—Eric Lindemann,[4] my colleague at Harvard, has carried out some interesting studies on the nature of the process of mourning which carry clear and specific implications for medical practice. He has found that a bereaved person goes through a well-defined process in adapting to the death of the relative, that this process usually takes four to six weeks to complete, and that it is characterized by a succession of specific psychological steps with accompanying emotional side-effects. It seems that when a key figure is removed by death or desertion from a person's life, that person has to work quite hard, psychologically, in order to adapt to the loss and in order to fill in the resulting emotional hiatus.

Lindemann also found that whereas the majority of people manifest these characteristic mourning reactions, which show they are satisfactorily doing their "grief work," and recover their psychological and psychosomatic equilibrium by the end of the four to six weeks, a small but significant group of bereaved people do not show these changes, or show them in distorted form; many of these people either immediately or later show definite and sometimes extreme signs of psychiatric or psychosomatic illness, particularly depression and disorders of the gastrointestinal tract, such as peptic ulcer or ulcerative colitis.

Lindemann postulates a direct causative link between the absence of a normal mourning process and the later development of these illnesses. He has also shown that sometimes these illnesses can be interrupted by helping the patients revive the problems of their bereavement and belatedly do their undone grief work.

Among the characteristic manifestations of a healthy mourning reaction are withdrawal of interest from the affairs of daily life and business, feelings of mental pain and loneliness, weeping, disorders of respiratory rhythm with frequently repeated deep sighs, insomnia, loss of appetite, and —most characteristic—preoccupation with the image of the deceased person, usually in connection with the revival of numerous memories of joint activities with him. Lindemann feels that this last phenomenon is the key to understanding the essence of the mourning process. The bereaved person withdraws his energy from most of the aspects of everyday life and concentrates it on reviewing, detail by detail, those aspects of his past life which were enriched by his association with the deceased. In each of these life segments he has to realize afresh the pain of his loss and rather concretely to experience its permanence. In each of these segments he has to make a special act of resignation to the inevitable. This can only be achieved through suffering, but not until it is completed can the person achieve mastery and independence in that segment of his life, so that he can return to normal activity and emotional stability.

Each bereaved person must do this grief work for himself, and mourning is a lonely process; but the traditions of most cultures illustrate to us that neighbors and friends and representatives of the larger community can help the mourner both by the general emotional support of condolence and by practices which permit him or encourage him to go through the steps of his grief work. In our modern culture the weakening of religious and other cultural systems of values and traditions has thrown many people largely on their own emotional resources, and the family physician is one of the people whose work may call him to step into the breach. In doing so in this area he may well try to enlist the support of the priest or clergyman or rabbi, each of whom has his own traditional approach to these problems.

In order to understand specifically what the family physician might do to help the bereaved person mourn successfully, it is helpful to list some of Lindemann's findings among the unsuccessful mourners, who later developed various illnesses. No single simple picture was characteristic of this group, but combinations of the following reactions were common. Instead of withdrawing interest from daily life many of them showed more business activity than usual and by diverting their interest to the problems of outside life appeared to escape the inner turmoil of mourning. They did not weep. They felt little or no pain, either saying they felt numb and empty or showing a strange cheerfulness. Many of them showed marked hostility, often directed toward the physicians and nurses who had cared for the deceased. In all cases there was an absence of preoccupation with the deceased, and on direct questioning many said they were quite incapable of recalling in memory the image of the deceased person. The over-all picture which was most commonly found was an attempt to deny the emotional importance of the whole business and to get on with problems of living without the burden of mourning. In the short run the external emotional manifestations of this group seemed easier and happier than the group of active mourners, but in the long run many of them paid very dearly for their temporary ease.

The guideline for the physician who wishes to profit from these studies is to try and help his patients grieve along the lines of the first group and to be particularly active in giving his help whenever he recognizes in one of his patients, during the mourning period, signs which resemble those of the maladaptive group. Experience has shown that to help such people grieve successfully it is not necessary to know the inner psychological reasons for their being hampered in this regard. The uncovering of these deeper complications is not necessary; all that seems important is to get them by whatever means to dwell on the image of the deceased and to go over and over in their minds the many activities which they shared with him in the past, in order little by little to realize that from now on he will be missing from their lives. What is also necessary is for the physician to give the patient the full measure of his emotional support and sympathy in bearing the pain of this process and for him to mobilize other sources of support within the family and outside it. In this regard the physician should realize that emotional support depends, among other factors, on the quantity of personal interaction, so he should realize the special importance of even short extra visits to his patient during the mourning period, or, if these are not possible under the pressures of a busy practice, at least of phone communication. Since the pathological sequelae of inadequate mourning are usually so severe, these extra visits are well worthwhile.

When the physician is not able on his own to stimulate a proper mourning reaction, when his efforts to enlist the aid of ministers of religion and members of the extended family also lead nowhere, and when mourning is absent or continues without apparent resolution long after the expected period of four to six weeks, the physician would be well advised to take active steps to refer the patient to a psychiatrist at that stage and not wait for the psychiatric illness to develop. This is a situation where a specialized "stitch in time" may well "save nine."

Other Crises.—Space does not permit me to go into detail about other examples of direct help by the physician to people in crisis, and I hope that some general principles may have emerged from my discussion of help with bereavement. I wish, however, to make brief supplementary mention of two other crises commonly met in medical practice, the crisis faced by parents who have to adapt to the realization that their baby has a congenital abnormality or is mentally defective and the crisis of a patient or his relatives having to adapt to a chronic or an incurable illness, a major disability, or to death itself. These situations all call for special activity on the part of the physician, in addition to the customary "frank" or "not so frank" talk.

The physician must face the fact that the impact of the news of the diagnosis is likely to be followed by a period of psychological reorientation similar to the grief work of the mourning period and interestingly enough also lasting for about four to six weeks. Patients and their relatives should not be expected to handle these psychological burdens on their own. They may need a good deal of support from the physician in facing the painful implications of the situation and help in avoiding facile escape into denial or obliteration of the problem by wish-fulfilling fantasies. The physician should try to help them keep the problem in consciousness during this period and deal with its implications piece by piece. It is remarkable the power that ordinary people have to adapt to reality, however unpleasant. It is not realities but dreams which "make cowards of us all," and insofar as the problem is allowed to sink into dreams and into fantasies it gets removed from the strength which derives naturally from our universal adaptive mechanisms.

On the other hand, the physician should realize that in its initial impact a problem may be quite overpowering and some partial or initial denial is a fundamental defense mechanism. He should not interfere with this, nor with the occasional rest periods during the adaptation process when the patient tries for a while to forget his problems by diverting his interest to other matters. In fact the physician who knows his patient may be able to recognize when he is becoming too fatigued by facing the unfaceable, and he may then prescribe a temporary respite by diversion or drugs. He should be on the alert, however, to call a return to the fray once the rest period has resulted in the replenishment of resources.

I would like to sound here a word of warning against the indiscriminate and continuous use of tranquilizing drugs for people in crisis. Studies are at present under way to determine not only their pharmacophysical ill-effects but also their possible psychological complications; among the latter I predict we will probably find that, by damping down too drastically the impact of crisis situations, tranquilizers may be preventing the active processes of healthy adaptation to important life difficulties and thus laying the stage for subsequent psychiatric illness.

Need for Psychiatric Consultation

The family physician who seriously wishes to enlarge the scope of his practical operations in order to cater to the mental health needs of his patients and their families would be well advised to build up a collaborative working relationship with a psychiatrist of his choice. If a psychiatrist is not available, such help can also be obtained from a well-trained clinical psychologist or a psychiatric social worker. The important thing is wherever possible to use the same person each time, so that the two can learn each other's language and ways of working.

In talking about consultation I do not have in mind the occasional necessity to refer a patient with some psychiatric illness to a specialist for investigation and treatment. This will certainly be necessary, and the more sophisticated the family physician becomes in dealing with emotional problems in his patients the earlier he will be able to identify such conditions and the more easily and surely he will be able to effect the referral procedure.

More Effective Understanding and Management.—The kind of consultation I am particularly referring to here is different: it is consultation by the general physician with the psychiatric specialist in order to enlist the latter's help in rendering the family physician's own understanding of the case and his own management of it more effective. However well trained the general physician may be, he will inevitably come across situations involving the emotional life of his patients which are outside the area of his previous learning and experience. The psychiatrist may, by discussing the case with him, be able to enlarge his understanding and to deepen his insight by pointing to the relevance of certain items of information about the field of forces which the physician had previously ignored. The psychiatrist's specialized knowledge of patterns of intrapsychic functioning and unconscious motivation may allow him to explain previously puzzling aspects of the patient's personality and that of his relatives which throw new light on their behavior and afford new opportunities for helpful action by the physician. It is very important for the doctor to tailor his intervention in the family to the special individual personality characteristics of its members. Most family physicians will build up a store of relevant knowledge of the weaknesses and strengths of their patients from their years of experience with them, but every now and again there will be some reactions which are quite unexpected and the physician may find his best efforts frustrated. On such occasions the psychiatrist's knowledge of the deeper unconscious aspects of personality functioning may clarify the situation so that the physician may find a new way to help his patient.

Improving Use of the Self.—Another type of help which the physician may expect from the mental health consultation is that of sharpening and improving his own use of the self in his professional medical functioning. A physician constantly makes use of different aspects of his personal influence on his patients as part and parcel of his daily work. This use of the effect of one human being who is being helpful on another who is in need becomes especially important in dealing with those needs which are predominantly emotional rather than physical.

Unfortunately, although physicians make use of personal influence all the time in their medical practice, this usually remains an amateur, somewhat haphazard set of operations with most physicians rather than a consciously directed professional therapeutic instrument. Some physicians have a more consistently therapeutic personal effect on patients than others, and we ascribe this to innate personality gifts or to a generalized "bedside manner" of uncertain origin. Even these physicians often fail in their efforts to support or stimulate or reassure certain patients, and when they fail they can no more understand why this has happened and deal with the consequences than they can understand their successful cases. The average physician is no better off when it comes to understanding his own special emotional reactions to certain patients—his feelings of liking and warm protectiveness, his irritability and anger, his frustration, his anxiety, or sometimes his guilty withdrawal. He does his best to control these feelings and not allow them to interfere with his objective medical approach, and his training usually helps him to succeed—but often at the expense of becoming rather distant and cold. It is the rare general physician who is able to capitalize consciously, both for diagnostic and for therapeutic purposes, on his awareness of his own feelings as they are stimulated by the behavior of his patient.

The psychiatrist, on the other hand, has by a long and arduous training not only learned to know and accept his own human reactions in his reciprocal interaction with his patients but he has learned to make explicit and differentiated use of them in the professional setting. Through the consultation process the physician may gain from him some understanding and skill in this matter. This will only come gradually, which is another reason for working with the same consultant over a lengthy period. This is not a matter of the giving or the receiving of intellectual prescriptions but the emotional education which comes from numerous discussions about the details of practical life situations and one's feelings about them.

Consultation, a Two-Way Process.—So far I have talked as though the psychiatrist were the teacher and the family physician the pupil in the consultations, and to some extent this is so; but the physician who imagines that all he will have to do is to ask questions and get the answers from the psychiatrist will be sadly disappointed. He will quickly discover that with all his specialized knowledge the psychiatrist does not have many answers to the circumscribed questions about the practical issues of management of ordinary patients in the situation of general practice.

I said before that mental health consultation is a joint collaborative endeavor, and what I meant to imply is that it has to be a two-way process, in which not only the psychiatrist but also the physician must be an active partner. It is essential for the physician to realize that he must take active steps to educate the psychiatrist during these consultations so that he will understand the special nature of the management problems involved, which will be quite different from what he is used to in the very unusual circumstances of his psychiatric clinic or office practice. Working with the same psychiatrist over a period of time the physician may be able to teach him enough about the daily problems of general practice and the life situations of ordinary people who do not consider themselves psychiatric patients that he can eventually get answers which come reasonably close to being useful, but he will usually have to work quite actively to take what the psychiatrist has to offer and to translate it for his own use.

A psychiatrist who has himself had experience in general practice before undergoing psychiatric training sometimes finds this type of consultation easier, but it is surprising how specialized psychiatric training and experience, which dwell constantly on the abnormal and the unusual and on unconscious motivation and irrational fantasy formation, impair the memories of this previous experience with the world of normality. A psychiatrist usually realizes the extent to which this is so and realizes and respects the degree of expertness of the family doctor's specialized knowledge in his own field only after he has been educated by his consultee.

I can vouch personally for the importance of this process because in the course of my own experience in community psychiatry I have been successively educated by social workers, public health nurses, pediatricians, obstetricians, and nutritionists, most of whom were initially a little surprised to find how much they were teaching me during their consultations.

Responsibility for Plan and Implementation.—This leads me to my last point. The management plan which emerges from the consultation may have been arrived at as a result of a fruitful joint collaborative endeavor, but the type of plan and the responsibility for its implementation must remain with the family physician and must fit into the general framework of his traditional methods of functioning. Both parties should beware of working out a psychiatrist's plan instead of a family physician's plan and of turning the physician into a "proxy psychiatrist." The style of work of the family physician is fundamentally different from that of the psychiatrist.

For instance, take the time relations of their professional work. It may seem that a busy general practitioner would never have the time to make use of the kind of knowledge I have been discussing in this paper; he could never spend the time which the psychiatrist can apparently allot to his small select group of patients. This is a red herring. It presupposes that, to cover the same problem, members of the two professional disciplines will use the same approach. This is neither necessary nor desirable, since the different professional roles have been differentiated over a long time in order to cope with problems in a very special way which has been found empirically to be effective and which is recognized by being embodied in the traditional culture of that profession. In this case, for instance, the practices of the psychiatrist in relation to time are based on the fact that his patients are strangers to him; since he has to penetrate below their surface defenses and deal with unrecognized and unacceptable material, his relationship with his patient, however intimate the content of their discussions, remains a highly structured stranger relationship, in which each takes care to keep outside the boundaries of each other's customary social life. The regular appointment and the 50-minute hour are derivatives of this situation, the interview between patient and psychiatrist being specially separated from the rest of the patient's life so as to give him the security to lay down temporarily some of his defenses. The length of the usual psychotherapeutic treatment is also dictated by the fact that the psychiatrist has to deal systematically with much complicated material in working down from the surface of consciousness to those hidden areas in which he searches for the unconscious sources of the illness.

The family physician by contrast knows many of his patients as friends. He has known them and their relatives for years, and even in the case of a new patient he can assume that this will be a prolonged contact. He does not need to collect important information about the personality of his patients in a few long highly structured interviews; it comes in dribs and drabs, either directly or indirectly from many and various collateral sources. He penetrates the patient's social life and home as a friend, and very often his patients come into his own home as a friend. Certainly he learns many secret and intimate things about his patients, but the level of such knowledge and the confidence in professional secrecy are such that this rarely leads to a patient feeling the need to hide from the physician in social situations.

Finally, one must realize that, in helping his patient handle emotional problems of the crisis type I have referred to, the family physician does not need to make long speeches. The most powerful interpersonal messages in which one person influences another are often very short. When the time is ripe at the height of the crisis, the right word or the right few words in the right place give better results than a lecture. Often it is a brief aside or an implication of some statement which ostensibly deals with some detail of management of a physical symptom which does the trick. Very often the most powerful messages are conveyed without words—by one's understanding manner, by one's patience, by one's warmth of greeting, or by a sympathetic nod or gesture. These do not take time, and these are the stock in trade of the physician. The results will be determined by their appropriateness in relation to the specific condition of the patient in his current predicament; but if success is only partial the family physician can always rely on being able to wait for additional opportunities in the future, since his relation with his patient will probably be continuing for many years to come. Through his consultations with the psychiatrist, he will gradually become more and more skillful in these areas. I believe that this skill is a main prerequisite for success in preventing emotional illness in our communities.

55 Shattuck St. (15).

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RESULTS OF ADDITION OF LIOTHYRONINE TO A WEIGHT-REDUCING REGIMEN

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The effectiveness of liothyronine as part of a weight-reducing program was investigated in a number of obese patients who were taking a standard 1,000-calorie diet. A preliminary study established 75 mcg. per day as a safe dose. The final study involved 57 patients who took the same diet together with a d-amphetamine-amobarbital preparation for two eight-week periods. Group 1 (28 patients) in addition received a placebo during the first period and liothyronine during the second, while group 2 (29 patients) received liothyronine during the first and the placebo during the second period. No significant difference was found between the two groups during the first period, but during the second period group 2 ceased to lose. Group 1, receiving liothyronine during the second period, continued to lose, and for this group the weight-reduction amounted to 0.39 kg. (0.86 lb.) per week for 16 weeks. Liothyronine was of great help to patients who could not maintain an adequate rate of weight loss on the established regimen.

Desiccated thyroid has enjoyed great popularity as a weight-reducing agent for many years by those who believe that diminished activity of the thyroid gland is a frequent cause of obesity. However, although a gain in weight has been attributed to a low level of metabolism, recent studies have demonstrated that hypothyroid and even myxedematous patients are not necessarily obese. Indeed, when the weight of their excess fluid is discounted, they may be underweight.[1] Thus hypothyroid patients are not necessarily obese, and most obese patients have normal thyroid function.

Thyroid has also been used as a "general metabolic stimulant" for the purpose of burning up excess fat. However, while the consistent, predictable effect of thyroid in increasing metabolism in myxedema is well known, its calorigenic effect in euthyroid persons is not so certain, and its use in the treatment of obesity has been disappointing. It has been demonstrated repeatedly that weight loss induced by means of thyroid hormone can only be accomplished by administering this drug in amounts sufficient to produce toxicity; the dangers inherent in prolonged treatment of this kind are obvious.[1]

Johnson and co-workers[2] studied the effect of increasing increments of thyroid in euthyroid patients and reported that it was extremely difficult to bring about a permanent elevation in the basal metabolic rate. On a dosage of 2 grains (0.12 Gm.) a day there was an early rise in the basal metabolic rate and then a gradual fall. When the dosage was increased to 4 grains (0.25 Gm.) daily the metabolic rate again rose, and on prolonged administration it again fell, but not to the original level. A few instances of toxicity were noted. On 6 grains (0.4 Gm.) a day there was again an increase in metabolic rate. The rate again declined, but became stabilized above the control level. Toxic symptoms were frequent. At a dosage of 6 grains daily some subjects began to lose weight but suffered from increased fatigability, malaise, and palpitation. There were great individual variations in the tolerance to thyroid among the subjects. Some could not tolerate 3 grains (0.2 Gm.) a day, while one patient noticed no ill-effects while taking 10 grains (0.6 Gm.) a day. This latter patient, incidentally, gained weight while taking such an enormous dose of thyroid.[2] Because the effect of thyroid in producing weight loss in euthyroid patients is inconstant and unpredictable, we have discontinued this use of it.

In line with the discussion of thyroid as a general metabolic stimulant, mention should be made of dinitrophenol. This drug was introduced in 1933 and enjoyed widespread but brief popularity as a metabolic stimulant for use in weight reduction. Theoretically, it should have been very effective because of its ability to increase selectively the oxidation of fat. However, because it produced a high incidence of toxic effects, it rapidly fell into deserved disrepute and its use has been abandoned.

Triiodothyronine differs from thyroxine in the absence of one iodine atom in the 5′ position (fig. 1). Three forms of the hormone have been found to exist: D-, DL-, and L-triiodothyronine. L-triiodothyronine, known as liothyronine, is the most active. It is three to five times as active calorigenically as thyroxine, depending on the method of assay.[3]

Liothyronine acts much more rapidly than thyroxine or desiccated thyroid. The effects of liothyronine become apparent clinically within 24 hours after administration. Similarly, the duration of liothyronine activity after cessation of treatment is about 2½ days, compared to from 6 to 12 days for

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thyroxine.[4] Liothyronine exerts a more rapid suppressive effect on the radioactive iodine uptake of the thyroid gland than does thyroxine, and its effects are more rapidly dissipated on discontinuation. For these reasons Werner feels that liothyronine is preferable for use in conjunction with the radioactive iodine uptake in differentiating euthyroidism from hyperthyroidism.[3]

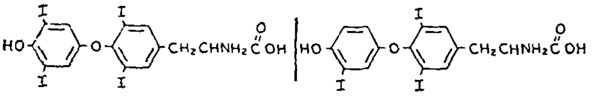

Fig. 1.—Chemical formulas for *left,* thyroxine, and *right,* triiodothyronine.

The level of the serum protein-bound iodine (PBI) is only slightly influenced by liothyronine. Starr and Liebhold-Schueck[5] found it produced a slight fall in PBI concentration. Thyroxine and desiccated thyroid, on the other hand, produce a rise in PBI concentration. The reason for this unusual effect of liothyronine is not known for certain. It has been attributed to (1) rapid egress of liothyronine from plasma into the peripheral tissue cells, (2) rapid degradation and excretion of liothyronine, and (3) lessened peripheral demand for hormone ordinarily produced by the thyroid gland, which results in a decrease in such production resulting from the inhibition of pituitary thyrotropin by liothyronine.

The exact synthesis of liothyronine in vivo has not been defined. It has been postulated that it is formed by the enzymatic deiodination of thyroxine in the peripheral tissues and that it is the active thyroid hormone.[6] Starr[5] believes that both thyroxine and liothyronine possess thyroid hormone activity. In normal situations thyroxine maintains caloric homeostasis, while under stress or emergency conditions liothyronine is produced at an increased rate from thyroxine.[5] Because liothyronine has been shown to produce a rapid calorigenic response, even in some patients refractory to thyroid or thyroxine, its effects in the management of obesity have been studied. Brügel and Riehm[7] found that diet plus liothyronine produced a greater rate of loss of weight than diet plus thyroid or diet alone. Weidenhamer[8] observed a group of obese patients presenting the clinical picture of "metabolic insufficiency." These were treated with diet and *d*-amphetamine, but after a few weeks weight loss had ceased or become negligible. Addition of liothyronine to the regimen resulted in a resumption of weight loss. In a detailed metabolic study of the effects of liothyronine in obese persons Bansi and co-workers[9] found that the average loss of weight resulting from use of this medicament was significant and surpassed the values attained prior to its administration.

Preliminary Study

These favorable reports aroused our interest in this use of liothyronine, and a double-blind study was planned to see whether the published results could be confirmed. However, before a double-blind study could be undertaken, it was important to know what dose would produce good therapeutic results without causing side-effects. It was also necessary to know whether the age, basal metabolic rate, and blood pressure of each subject would influence this dose, and so we conducted a preliminary study.

Fifty-five outpatients at the obesity clinic of the Metropolitan Hospital, New York City, were selected for the preliminary study. The standard clinic 1,000-calorie diet was prescribed for all patients. In addition liothyronine was prescribed in an initial dosage of 25 mcg. a day. Patients were seen biweekly, at which times they were asked about the development of side-effects. If none were manifest, the dose was increased by 25 mcg. daily. If side-effects had developed, the dose was decreased by 25 mcg. or more depending on the severity of the side-effects. In this manner the maximum daily dose of liothyronine which would not cause side-effects was determined for each patient.

When the amount of liothyronine administered each day exceeded the tolerable amount, all patients developed one or more mild side-effects. The side-effects were nervousness in 11 patients, tachycardia in 10, hunger in 8, palpitation in 7, insomnia in 7, dizziness in 4, headache in 4, angina in 2, abdominal distress in 2, and shortness of breath, tremors, leg cramps, and vomiting in one patient each.

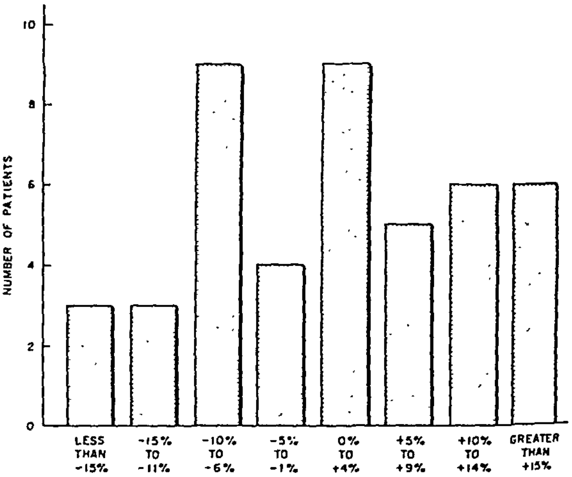

Fig. 2.—Distribution of basal metabolic rates before therapy in patients in first study.

At each return visit, the patients' weight, pulse rate, and blood pressure were recorded. A determination of the basal metabolic rate was requested for each patient prior to the initiation of liothyronine medication, for the sake of completeness of the data as well as to satisfy our curiosity. The results are depicted in figure 2. We are aware that basal metabolic rates cannot be reliably determined by the standard procedures for this measurement in obese persons,[3] but we were interested in learning whether there was any correlation between the basal metabolic rate prior to liothyronine therapy and the rate of weight loss. No such correlation was found (table 1). For this reason, and because in previous studies we had not been able to demonstrate any significant change in basal metabolic rate during weight reduction in a similar group of patients with use of the same diet,[10] the basal metabolic rates were not determined in the subjects whom we subsequently used in the double-blind study.

Table 1.—*Average Weight Loss for Patients in Preliminary Study Related to Basal Metabolic Rate*

	No. of Patients	Av. Time Observed, Wk.	Av. Weight Loss, Lb./Wk.
BMR			
More than −5	30	6.7	0.9
−5 or Less	15	6.9	1.1
Not recorded	10	6.4	1.1
Over-all average	55	6.5	1.0

The distribution curves of the maximum daily dose which could be tolerated without side-effects peaked sharply at 75 mcg. The mean dosage was slightly more than 75 mcg. a day. When the data were analyzed for effects of basal metabolic rate, age, or systolic blood pressure, it was found that patients with a basal metabolic rate of less than −5 who were less than 45 years old and who had systolic blood pressures below 150 mm. Hg were able to tolerate slightly larger doses of liothyronine than could other patients. The differences, however, were small (fig. 3, 4, and 5). An interesting side light of this preliminary study was that liothyronine produced an average weight loss of 1 lb. (0.5 kg.) per week (table 1).

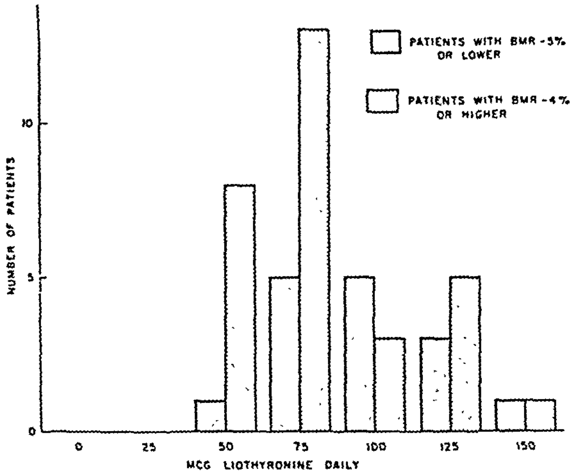

Fig. 3.—Maximum tolerated daily dose of liothyronine as related to basal metabolic rate in patients in first study.

Double-Blind Study

Material and Methods.—This double-blind study was planned to compare the efficacy of a capsule containing *d*-amphetamine and amobarbital in a sustained-release form with a combination of this capsule and liothyronine for the management of obesity under clinical conditions. Fifty-seven patients completed the study, 54 women and 3 men. Their average height was 62.8 in. (159.4 cm.), average weight 193.5 lb. (88 kg.), and average age 43 years. The usual 1,000-calorie clinic diet was prescribed for all patients. This diet allowed 75 Gm. of protein, 100 Gm. of carbohydrate, and 40 Gm. of fat per day.

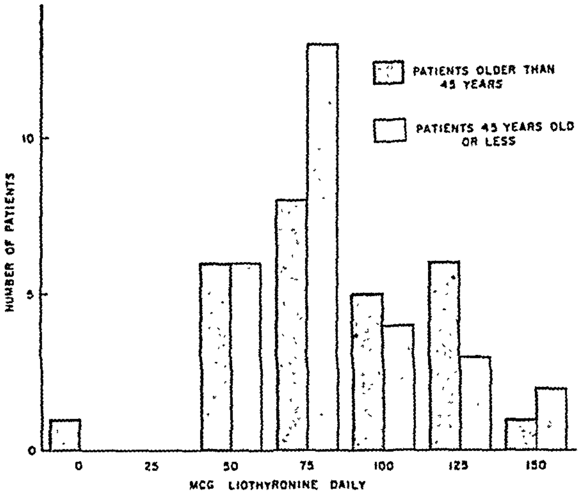

Fig. 4.—Maximum tolerated daily dose of liothyronine as related to age in patients in first study.

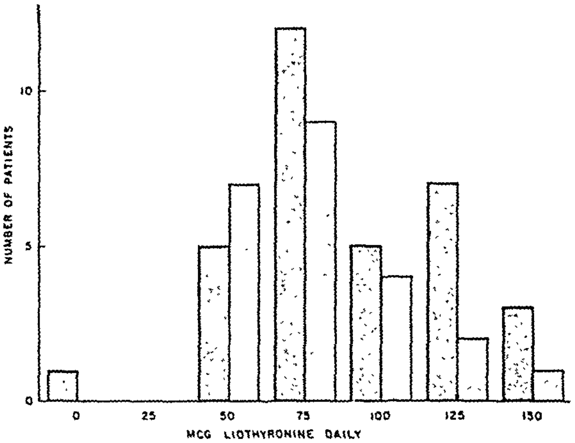

Fig. 5.—Maximum tolerated daily dose of liothyronine as related to systolic blood pressure in patients in first study. *Left-hand columns,* patients with systolic pressure below 150 mm. Hg; *right-hand columns,* patients with systolic pressure 150 mm. Hg and above.

The study was arranged so that half of the patients were started on the regimen of the *d*-amphetamine–amobarbital capsule and half on the combination of this capsule and liothyronine. Schedules were exchanged after eight weeks, so that each patient received each regimen for eight weeks and thus served as his own control. The liothyronine was supplied in pink capsules containing 25, 50, and 75 mcg. of the drug. The *d*-amphetamine–amobarbital preparation was supplied in brown sustained-release capsules containing 10 mg. of *d*-amphetamine and 65 mg. of amobarbital. In the combination regimen the liothyronine doses were increased as follows: weeks 1 and 2, 25 mcg.; weeks 3 and 4, 50 mcg.; weeks 5 and 6, 75 mcg.; and weeks 7 and 8, 75 mcg.

TABLE 2.—*Average Weight Loss, Blood Pressure Level, Pulse Rate, and Cholesterol/Ester Level for Patients in Double-Blind Study*

	Period		
	Pretest	1	2
Weight loss, lb. per wk.*			
Group 1		1.14	0.84†
Group 2		0.88†	0.01
Blood pressure, mm. Hg			
Group 1	137/89	134/85	138/85†
Group 2	143/87	140/86†	149/88
Pulse rate, beats/min.			
Group 1	80	86	86†
Group 2	82	88†	84
Cholesterol/ester level, mg./100 cc.‡			
Group 1		300/179	320/192†
Group 2		271/172†	304/181

* Totals: group 1=0.86; group 2=0.58 lb.
† Liothyronine regimen
‡ Group 1=20 patients; group 2=17 patients.

During the period when liothyronine was not given patients received the placebo capsule. Thus the patients took one brown and one pink capsule once each day during the entire 16-week period of observation. The drug coding was arranged so that the liothyronine titration progressed unnoticed, and the investigating physicians did not know the order in which regimens were employed until the completion of the study.

Patients were seen every two weeks. At each visit they were weighed, had their pulse rate and blood pressure recorded, were questioned about their appetite and appearance of side-effects, and were given a new supply of medicaments. In addition serum cholesterol and ester levels were determined in many of the patient during each regimen.

Throughout the description of the results reference will be made to period 1 and period 2 and group 1 and group 2. Period 1 refers to the first eight weeks and period 2 to the second eight weeks of observation. Group 1 consisted of 28 patients who were given *d*-amphetamine–amobarbital during period 1 and this plus liothyronine during period 2. Group 2 consisted of 29 patients who received combined therapy during period 1 and *d*-amphetamine–amobarbital therapy alone during period 2.

Results

Weight Change.—A statistical difference between regimens is demonstrated. The responses in period 2 which favor the combination are fully responsible for this difference (table 2). Statistical tests show no significant difference between the losses of 1.14, 0.88, and 0.84 lb. per week. The total weight loss by weeks for each group is demonstrated in figure 6. Loss of weight ceased after the eighth week in group 2. However, the rate of loss of weight on the combined therapy with liothyronine is relatively constant over the entire study period.

Blood Pressure, Pulse Rate, and Serum Cholesterol and Ester Levels.—Comparison was made between the pretest blood pressure level and pulse rate and those determined at the end of each test period for each group. No significant effect on the blood pressure could be demonstrated by any of the medicaments in the dosages employed in this study, nor was there any significant effect on the pulse rate (table 2).

Considering the large variation from patient to patient, and the technical difficulties inherent in the determination of the level of serum cholesterol,[11] the results are remarkably constant (table 2). Statistical analysis did not reveal any significant differences between the therapeutic regimens in this respect.

Appetite.—At each visit patients were asked about the effect of the medicament on their appetite during the preceding two weeks. An increase in appetite was recorded as a plus figure, and a decrease was recorded as a minus. The scores ranged from +2, moderate increase, to −3, marked decrease. We realize that appetite is purely a subjective phenomenon, and this attempt to quantitate it is of questionable scientific accuracy. We include the

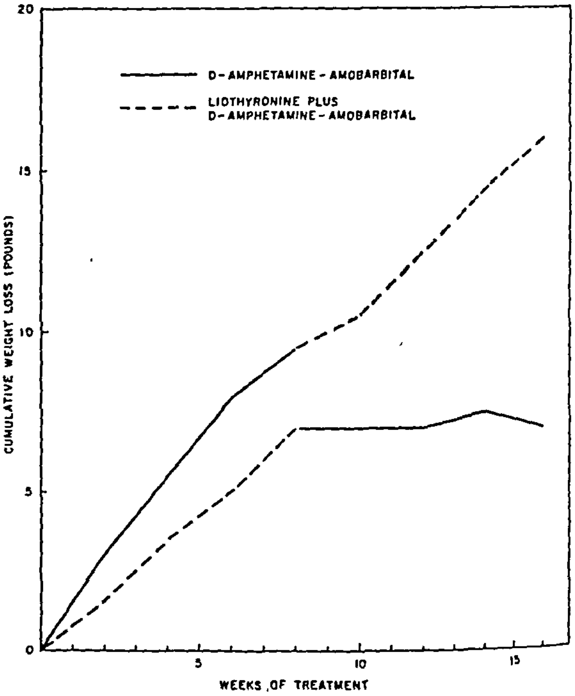

Fig. 6.—Total cumulative weight loss by weeks for all patients in double-blind study.

results merely for the sake of interest and curiosity.

The appetite scores agreed with the weight loss data: For group 1 the average appetite score for period 1 was -0.92 and for period 2 (liothyronine regimen), -0.60. For group 2 the score for period 1 (liothyronine regimen) was -0.52 and for period 2, -0.16. The only statistically significant finding was the very low score (0.16) which occurred in group 2 during period 2.

Comment

The data indicate that both regimens produced equivalent weight changes for the first eight weeks. Thus, the addition of liothyronine added nothing in the early weeks of the study. The last half of the study presented some interesting data favoring the addition of liothyronine. When the combined therapy was given after the *d*-amphetamine–amobarbital preparation alone, weight loss continued at the same rate. Thus these patients continued to lose about 1 lb. (0.5 kg.) per week throughout the entire 16-week period of observation. When *d*-amphetamine–amobarbital was prescribed after the combination with liothyronine, very few patients continued to lose weight and some began to gain. The average weight change for this group of patients was about zero.

In a previous study [12] it was found that when large doses of *d*-amphetamine are given to patients with no dietary restriction, an average loss of weight of at least 1 lb. a week can be maintained for only about eight weeks. After eight weeks there is a rapid decrease in the rate of weight loss.[12] This finding is very similar to the results obtained with the patients in group 2 after the first eight weeks of observation.

Liothyronine may be of help to those patients whose weight begins to level off while on one of the usual weight-reducing dietary regimens. This is exactly what we found in the studies of Brügel and Riehm,[7] Weidenhamer,[8] and Bansi.[9] Their procedure was to prescribe liothyronine after their subjects stopped losing weight. These investigators found that their patients again began to lose weight when liothyronine was added to the basic regimen.

The reason for this effect of liothyronine is obscure. Several investigators have found a decrease in metabolic rate in obese patients on caloric restrictions.[13] It has been suggested that liothyronine prevents this fall in the metabolic rate. However, Werner [14] pointed out that it is not known whether the basal metabolic rate can be increased by the administration of thyroid to obese patients, and many investigators believe that thyroid alone is ineffective in the management of obesity.[15] If it were simply a matter of maintaining the level of metabolism, thyroid should be as effective as liothyronine. Also, it is not universally accepted that calorie restriction in the obese person will result in a fall in the metabolic rate. Rynearson and Gastineau [16] believed that the protein content of the diet is important and stated that it is possible that a generous supply of protein may prevent this fall in the basal metabolic rate. In previous studies we have not been able to demonstrate any significant change in the basal metabolic rate during weight reduction in a similar group of patients with use of the same diet.[10]

With use of much larger doses of liothyronine than were employed in this study Brügel and Riehm [7] and Bansi and co-workers [9] caused a mild degree of hypermetabolism in their patients as measured by the basal metabolic rate and radioactive iodine uptake. Although such determinations were not performed, we noticed no clinical evidence of excess thyroid activity. Certainly no effect on the pulse rate or blood pressure was apparent.

Since the patients in group 2 received the combined therapy with liothyronine initially, it may be questioned whether there could have been a depression of the thyrotropic hormone of the pituitary by the liothyronine. Thus there might have been a lowering of metabolic rate during period 2, which resulted in the failure of these patients to continue to lose weight. It is hardly likely that if there had been such an effect it would have persisted for the entire eight weeks of period 2. After discontinuation of the administration of desiccated thyroid the thyroid gland regains its own function within three or four weeks.[2] The effects of liothyronine are dissipated even more rapidly.[3]

Liothyronine in the dosage we employed did not influence the level of serum chloresterol. Bansi and co-workers [9] reported a considerable reduction in the serum cholesterol level after administration of liothyronine to a group of euthyroid patients. However, he employed an average dosage of 150 mcg. a day, twice that used in this study. Whether liothyronine exerts its effect in weight reduction by correcting a metabolic defect, by stimulating metabolism, by a diuretic effect, or by some as yet unknown mechanism is not apparent.

Summary and Conclusions

The efficacy of therapy with a *d*-amphetamine–amobarbital preparation was compared to therapy with a combination of these drugs and liothyronine when prescribed for the management of obesity. A group of 57 obese patients were studied under clinic conditions with use of a double-blind procedure. Each patient was observed for eight weeks on each therapeutic regimen. Twenty-nine patients received the combination with liothyronine initially, and 28 patients received the liothyronine therapy last. A 1,000-calorie diet was prescribed for all patients.

The two therapeutic regimens produced equal weight changes for the first eight weeks. When the liothyronine combination was given during the second eight weeks of the study, loss of weight continued at the same rate. However, when the liothyronine combination was given initially, there was no further weight loss during the latter eight weeks of therapy with the *d*-amphetamine–amobarbital preparation alone. Thus liothyronine may be of great help to those patients who cannot maintain an adequate rate of weight loss while on a weight-reducing regimen.

At the dosage level of liothyronine used in this study (up to 75 mcg. a day) no effect on the pulse rate, blood pressure, or serum cholesterol level was noted. No symptoms of hypermetabolism attributable to the liothyronine, such as nervousness, palpitation, or tremors, were elicited.

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The *d*-amphetamine–amobarbital preparation was supplied as Dexamyl Spansule No. 1 and the liothyronine as Cytomel by Smith Kline & French Laboratories, Philadelphia.

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RINGWORM INFECTION OF SCALP.—In 1941 an epidemic of a highly unpleasant ringworm infection of the scalp of children swept through the major cities of the United States. The epidemic started in New York, and soon after its arrival in Chicago involved about thirty thousand children here. The peculiarity of this infection, caused by the fungus Microsporon audouini, is that it clears spontaneously in adolescence and that the scalp hair of adults is immune to it with very few exceptions. . . . We found that human hair fat contains a large amount of free fatty acids (up to 30 per cent of the total weight of surface fats consists of free fatty acids) and that the free fatty acids inhibit the growth of fungi, especially that of Microsporon audouini. . . . The spontaneous cure of this infection during adolescence can be explained as follows: With the puberal development of sebaceous glands, the amount of sebum poured on the surface of the scalp increases threefold. Thereby the free fatty-acid concentration per surface area is raised beyond the critical level at which Microsporon audouini is able to thrive. The fungistatic sebum enters the loose parts of the superficial horny layer and the hair canals. Once there, it sterilizes all the pathways of the infection. It does not kill the fungi inside the infected hairs because, unlike the fungi, the fatty acids are unable to penetrate the hair shafts. However, the infected hairs are lost in the course of natural shedding, and the newly growing hair is no longer infected because all pathways have been sterilized. Thus a spontaneous cure takes place about two years after adolescence has set in, and thereafter the scalp is immune to this infection.—Stephen Rothman, M.D., Basic Research in Dermatology, *Bulletin of the Alumni Association, School of Medicine, University of Chicago,* Spring, 1959.

MODERN MANAGEMENT OF OBESITY—THE "SOCIAL DIET"

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One hundred consecutive, unselected patients with clinical obesity were classified as to the etiology of their condition. Overeating was accepted as the cause in 82, but in 18 cases this explanation was not satisfactory. The latter were mostly complicated cases of endocrine or metabolic disease. Satisfactory reduction (loss of 10% or more) of body weight was accomplished in 63 of the 82 and in 5 of the 18 by caloric restriction of diet. Simply reducing the portions of everything by about one-quarter enabled the patients to eat normally with inconspicuous modifications of the "social diet." Underlying emotional problems, if obvious to the practitioner, were treated by surface psychotherapy; if they were deep-seated, the patient was sent to a specialist. The author suggests medication with mild sedatives or anorectics as helpful during the period while new eating habits are being established.

Obesity has become an increasingly urgent health problem. The steady rise in the standard of living, including richer diets, mechanized transportation, audience rather than personal participation in sports, and automation, has helped to raise the number of calories taken in and lower the number of calories expended. The American population has for some time been growing sluggish and overfed, and only recently have there been signs of a swing in the other direction. Several fortunate circumstances have combined in the past decade or two to bring this problem sharply into focus and to lead to corrective action: overweight is now recognized as a threat to good health and long life, and the dictates of fashion have brought the slim figure back to popularity. Patients and nonpatients alike now seek advice about measures to control weight.

This has made the task of the physician somewhat easier. Experience has taught us that the most important factor in success in weight reduction is adequate motivation on the patient's part. If he is convinced that it is in his interest (health, appearance, or employment) to lose weight, he will usually make the necessary adjustments and even sacrifices. The factors already mentioned help establish this motivation, but the physician must reinforce these, keep encouraging his patient, and search out arguments applicable to individual cases.

For example, the physician will seek the reasons for the occurrence of obesity in the first place. One of the significant advances of the 20th century has been the demonstration (such as by Bruch[1] and others) of the importance of psychogenic mechanisms. The myth of the good-natured fat man has been finally exploded; he has been shown to have, more often than not, more than the average man's share of tensions and frustrations. It is now known that anxieties are more likely (except for short episodes) to result in nibbling than starvation and more likely to drive a man to food than to drink. In a short article, it is plainly impossible to list all the ways in which motivation may be established; it is enough to say that if a patient is convinced he should lose weight the specific problems of constructing a diet become relatively easy.

In making up a reducing plan for his patient, the physician must heed many factors or he will fail. Among these are the important sociological and cultural factors; for example, the national background must be reckoned with. If the patient or his parents are recent immigrants, plumpness may be valued for esthetic reasons or as evidence of successful emergence from poverty and hunger. It may be almost impossible to convince a foreign-born mother that heaviness is not a blessing or that tuberculosis does not invariably follow loss of weight. Ethnic factors in food selection must be recognized. An excellent article on the diet of Italian-Americans underscores this problem.[2]

Aside from personal and cultural food preferences, other factors must be taken into account.[3] The subject's basic requirements in fats, proteins, carbohydrates, minerals, and vitamins must be met, usually within the daily diet, although vitamin supplements are often necessary. The "satiety values" of food vary among themselves and from subject to subject. For example, meats are "satisfying" to most people, and I suspect that the success of bananas in many reducing diets, including the classic one of Harrop, is the result of its ability to "fill" the patient adequately. The "fetish value" of foods must be considered; in the popular mind, meat is sometimes equated with virility and spinach with the accumulation of "good, rich blood." This sort of prejudice will obtrude itself but seldom get in the way of establishing a sat-

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isfactory dietary regimen. Exercise should be encouraged but should not be depended on for weight reduction without calorie restriction.

In a review of 100 consecutive, unselected cases of clinical obesity, a grouping has suggested itself without much difficulty:

Group 1—Obesity unassociated with overeating (18 cases). These were mostly complicated cases of endocrine or metabolic disease.

Group 2—Obesity associated with overeating (82 cases), subdivided into (*a*) those in whom motivation and cooperation were easily established (51), (*b*) those in whom motivation and cooperation were established only after initial resistance (17), and (*c*) those in whom motivation and/or cooperation were absent (14).

The results of treatment with dietary regimen to be described were as follows:

Group 1—5 of the 18 patients had satisfactory reduction (loss of 10% or more of body weight).

Group 2—49 of 51 patients in subgroup *a* had satisfactory reduction, 12 of 17 in subgroup *b* had satisfactory reduction, and 2 of 14 in subgroup *c* had satisfactory reduction.

It seems obvious that the dietary management of obesity is evolving today in much the same way as that of diabetes some 20 years ago. In the latter case, the use of highly artificial diets with special preparation—specially, sometimes exotically, prepared dietetic foods, mostly canned; and synthetic foods or food substitutes—has been superseded by diets as closely resembling the patient's former diet and those of his friends and family as possible. A similar evolution is taking place in the management of obesity, artificial and complicated regimens being replaced by those which throw less burden on his family and enable the patient to become a more acceptable member of society. Except among persons who are obsessed with concerns of health and diet, there are few things more of a nuisance to a host than to have a guest discuss his diet or to be forced into preparing separate dishes for him—only one's own diet is of real interest!

A few precautions must be taken. It is inadvisable to prescribe a reducing diet for a short time, such as a month or six weeks; prescribing a diet on a piecemeal basis leads eventually to disappointment or backsliding. The dieter should realize that he will have to change his habits for a long time; in some instances, the struggle against adiposity is a lifelong one. The arguments against excessive weight may be put strongly, but neither the words nor the attitude of the physician during the dieting period should be such as to suggest punishment or to result in guilt feelings. Reinforcement of good intentions and gentle prodding or praise are usually sufficient. Many of the emotional problems of obese persons are obvious to a general practitioner and will respond to surface psychotherapy; problems which seem to be more deep-seated, as evidenced by resistance or hostility, or which seem to involve complex family relationships should be avoided and the patient should be sent to a specialist.

The Social Diet

The patient is instructed to eat normally with only a few modifications when the "social diet" is used. Not more than one slice of bread is to be eaten at any meal. At breakfast, the patient may have cereal or one slice of toast—not both. A small portion of rice, noodles, cracked wheat, or spaghetti and a small baked potato or a portion of peas or lima beans at dinner will add variety to the lean meat, green vegetable routine. No gravies are to be added to foods. Portions of everything are to be reduced by about one-quarter. If possible, portions should be smaller than those previously taken, and "seconds" must not be taken. Desserts are to consist of one portion of fresh fruit, 1 oz. (28 Gm.) of cheese, or a small slice of angel food cake. Suitable supplementary reading may be recommended.[4] On this regimen, almost every determined patient will lose weight. In the New York City area, it was found in 100 successive patients that this resulted in a reduction of about 1,400 calories. In many instances, the patient's friends—and sometimes his family—did not know that he was on a diet.

In any case, when a new dietary regimen is prescribed for obesity or, for that matter, any other condition such as heart disease, diabetes, or hypertension, the dieter may need a medicament to help suppress his appetite. When newer eating habits are well established and accepted, the supportive medicine can often be withdrawn. In some instances, a mild sedative, such as phenobarbital or meprobamate, may suffice. More often, a stronger anorectic is needed; the drugs with which I have had most experience are the amphetamine series.

Anorectic agents of this type have been subjected to some adverse criticism recently, but studies by myself and careful double-blind experiments conducted by Fazekas and co-workers[5] have demonstrated that they have a genuine therapeutic action not to be explained by suggestion or placebo effect. Evidence which these authors review demonstrates that pronounced changes in satiety may be induced by lesions of the subcortical areas, particularly the hypothalamus. A reciprocal relationship may exist between the appetite-stimulating center and the appetite-inhibitory center, and changes in either of these may result in alterations of satiety.[6] The drugs may act on these areas by influencing localized neurohormonal activity.

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The amphetamine combination used in this study was supplied as Obetrol by Obetrol Pharmaceutical, division of Rexar Pharmacal Corp., Brooklyn, N. Y.

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SCOPE AND INTERPROFESSIONAL RELATIONS OF OCCUPATIONAL MEDICINE

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The subject of this paper is the scope of what occupational health encompasses or should encompass and what sort of relations obtain or should obtain between physicians engaged in this work and their confreres in the private practice of medicine. First, clarification should be made of the terms used to denote the several disciplines and activities involved in ministering to the health of the working man. The American Medical Association council is called the Council on Industrial Health. The principal specialty society of physicians serving industry is called the Industrial Medical Association. However, the specialty for which certification is now given qualified physicians by the American Board of Preventive Medicine is called occupational medicine rather than industrial medicine. Industrial nurses are beginning to call themselves occupational health nurses. Industrial hygienists, however, still cling to their title and have not yet called themselves occupational hygienists. "Occupational" is a broader term than "industrial" as the latter connotes industry, particularly manufacturing, whereas the former includes all "occupied" or employed persons, whatever the nature of their employment. We have to avoid, however, the extreme of having occupational health services cover all persons who "work" since, in the physiological sense, breathing is "work" and, *ipso facto,* the clientele of occupational health services could then be made to include all persons who breathe. Our confreres in private practice could not be blamed if at this point they rose up in righteous wrath.

Occupational health is preventive medicine in the working environment. The industrial physician gives attention to the healthfulness of the conditions and materials of the work and performs certain services; the latter embrace physical examinations, referral of patients to their family physicians when nonoccupational disease is found, health education and counseling, emergency or palliative treatment for certain nonoccupational conditions, immunization against diseases to which workers are occupationally exposed, and certain nonoccupational preventive health services. There must be free communication and mutual understanding between plant physician and family physician. In situations requiring mediation by a third party the county medical society's grievance committee should hear both sides. The problems and procedures of the industrial physician should be set forth at meetings under the auspices of state medical societies. Such presentations help to foster good relations between plant and family physicians.

The term "occupational" is really a better term than "industrial" as it refers to white-collar as well as blue-collar workers, persons employed in service, commercial, and business establishments as well as persons working in nuts and bolts factories, and farm and government workers as well as foundry workers. It follows, then, that "occupational health" is the proper term to denote those services carried

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on for the protection and promotion of the health of employed personnel; "occupational medicine" properly denotes the physician's role therein and "occupational health nursing," the nurse's role. The industrial hygienist retains his same designation but has an area of coverage coextensive with that of the physician and nurse.

Scope of Occupational Health and of the Physician's Activities Therein

A publication entitled "Scope, Objectives and Functions of Occupational Health Programs" was prepared by the Council on Industrial Health two years ago, approved by the Board of Trustees, and adopted and promulgated by the House of Delegates of the American Medical Association as an official policy statement of the Association.

Health Protection and Promotion.—Occupational health is defined as essentially preventive medicine—health protection and promotion—in the working environment. It affords benefits to the personal health of the worker but only as a by-product, as it were. Occupational health properly includes (1) detecting, evaluating, and correcting hazards to health posed by the environment in which, and the materials with which, the employee works and (2) examining the employee medically at suitable intervals to place him at work he can perform efficiently and with safety to himself and others and discover promptly any health impairment attributable to his work. If, in the course of such occupational health examinations, health defects not attributable to work are found, and the worker, being apprised of them, has them cared for by his family physician, the worker realizes a personal health benefit, but only as a by-product.

Health Education and Counseling.—Health education and counseling are also properly included in an occupational health program.

Treatment.—Definitive treatment of nonoccupational illness and injury is not properly a function of occupational health programs. Palliative, nonrepetitive, or emergency treatment of any condition may properly be performed in an occupational health program. Definitive treatment of occupational illness and injury, while properly included in an occupational health program to the limits imposed by its personnel and facilities, is really not a part of occupational health, which is essentially a preventive medicine, health protection, and promotion service in the working environment.

Screening Procedures.—Procedures designed to uncover evidence of nonoccupational health impairments, such as degenerative, metabolic, and malignant diseases, are in considerable vogue, particularly multiphasic screening procedures applied to various groups of people, including employee groups. Strictly speaking, these do not fall within the scope delineated for occupational health programs in this American Medical Association publication on "Scope, Objectives and Functions of Occupational Health Programs." However, few medical societies would object to plant medical departments' performing such procedures on plant employees, particularly if employees who, through such procedures, showed evidence of possible nonoccupational health impairment were referred to their family physicians for definitive diagnosis or, at least, definitive treatment. In defense of plant medical departments' doing these procedures, someone is likely to cite the example of the secretary in a plant who was found, on cytological examination of a uterine cervical smear, to have cancer in a sufficiently early stage to permit successful treatment. The implication is—and possibly it is the correct one—that had she not been examined then and there, her cancer might not have been discovered until it was too advanced to be cured. Then there is posed mutely, if not voiced, the rhetorical question, admitting, of course, of only one answer: Would it have been better had she not been given this test? Until physical examinations or screening procedures of apparently well persons are practiced to a more desirable degree of consistency and regularity in physicians' offices and other community health facilities, it would seem callous to prohibit their performance by industrial medical departments. However, medical societies will have to address themselves to this problem, and it is hoped that they will find a solution agreeable to all concerned and in the best interests of the health of the people.

Immunization.—Immunization poses a comparable problem. To what extent is an industry justified, warranted, or beholden to offer its employees immunization procedures as part of its occupational health program? Certainly there can be no gainsaying that an industry should offer its employees available immunization procedures against such diseases as they are peculiarly exposed to by the materials with which and in the countries or places in which they have to work.

Many other criteria are advanced for guiding an industry in immunizing its employees. Some of the most liberal industrial physicians claim that any available immunization procedure whatsoever should be offered employees for the sake of their health. Others, while not going this far, hold that whenever a disease, even one not peculiar to the place or conditions of work, threatens a plant's output, the plant is warranted in offering its employees immunization procedures against this disease, if there are any. Others hold that the criterion should be not simply the threat of the output, per se, of a plant, company, or other establishment, but the curtailment or suspension of the delivery of services or goods vital to the health, safety, welfare, or economy of the public, such as food manufacturing and delivery, public health services, police and fire protection, water, gas, and electric services, and public transportation. Here, again, medical societies should come to grips with the problem, and it is hoped that they will find a solution satisfactory to all concerned. Such solution should recognize that the prevention as well as the detection and treatment of nonoccupational illness is primarily within the province of the private practice of medicine but that there are times and situations where the job to be done in immunization is so great, and the means wherewith and the time in which to do the job so limited, that all available hands must help.

"Courtesy" Services.—It seems to be a common practice for an industrial dispensary to perform, as a "courtesy" to private practitioners, various personal health services, particularly diagnostic, for those patients of these private practitioners who work in the plant. The physician is at some disadvantage when his patient comes to him and says, "I can get this blood test in the dispensary of the plant where I work, if you will give me a note to authorize it." The implication is that if the physician does not oblige he is denying his patient something which the patient has coming to him for nothing and which he possibly could get another physician to authorize. The physician, then, is likely to permit such services to be performed as a "courtesy" to him. Some medical societies, however, have inveighed against this practice, adducing various reasons. One has threatened with disciplinary action any of its members who accept from industrial dispensaries such services for their patients. Here, again, medical societies must find the solution to this problem, hopefully keeping all concerned happy.

Summary.—The scope of occupational health programs is seen, then, to embrace at any given time and in any given location so much of the following as local needs require and as the cognizant medical society approves: (1) attention to the healthfulness of the place, conditions, and materials of work and (2) such services for workers themselves as (*a*) preplacement and periodic physical examinations to insure their placement in work they can perform efficiently and with safety to themselves and others and to detect any health impairment they may sustain from their work; (*b*) referral to their family physicians for nonoccupational health conditions found; (*c*) health education and counseling; (*d*) treatment, largely emergency, palliative, and nonrepetitive, for nonoccupational conditions and treatment within the capabilities of the plant medical personnel and facilities for occupational conditions; (*e*) immunization against diseases to which they are occupationally exposed; and (*f*) such nonoccupational preventive health services—as immunization and multiphasic screening tests—as are currently in vogue in the community.

The physician is generally considered the captain of the team that carries out such programs. Other team members are the industrial hygienist or industrial hygiene engineer, who looks to the healthfulness of the work environment, and the industrial nurse or occupational health nurse, who acts for and under the direction of the physician, assisting him in the performance of physical examination procedures and other services on the person of the worker, imparting health education and counseling, maintaining records, and in many other ways running the dispensary.

Interprofessional Relations

Professional relations between physicians in occupational health and their confreres in private practice will be determined largely by the extent and effectiveness of the communications between the two groups and by the extent of their adherence, individually and collectively, to the golden rule. In short, the industrial physician has to get the attention of his confrere in private practice, and the latter has to give his attention, to the end that all physicians are acquainted with the proper scope, objectives, and functions of occupational health programs.

Application of the Golden Rule.—Physicians associated with occupational health programs must scrupulously keep within this proper scope and perform only proper functions at all times. In so adhering to the golden rule, the industrial physician can come with "clean hands" to his confrere in private practice and rightly expect him to reciprocate in kind, to cooperate with him in the many ways required to insure the success of the occupational health program. The private practitioner, for instance, it is hoped, would be more careful and conscientious in issuing to the plant's employees notes entitling them to sick leave and would recommend only so much sick leave as required for strictly health reasons. It is hoped that the plant physician and family physician would communicate freely with each other about the health of their employee-patient. It is hoped that they would exchange their physical and laboratory examination findings and their clinical impressions, even their recommendations for the round-the-clock, day-in-and-day-out management of the case. The employee-patient concerned would benefit enormously, far more than were his family physician and plant physician otherwise disposed.

The family physician, further reciprocating the plant physician's adherence to the golden rule, would avoid the altogether too common practice of ascribing to a patient's work environment, solely by the process of elimination, illness or symptoms for which no other cause is found. Rather, he would contact the plant physician, tell him of the nature of the employee-patient's illness and of the failure of examinations to discover the cause, and ask the plant physician whether anything in the work environment in the plant could possibly account for this illness. This would be in accord with the injunction that Bernardino Ramazzini, the 18th century "father of occupational medicine" gave physicians when he advocated that, in addition to the questions propounded by Hippocrates, physicians ask their patients one other, "What is your work?"

The family physician, meeting the plant physician halfway, would also refrain from giving to the employee-patient whom he discharges from his care to return to work such impractical advice as, for instance, to do "light" work. Rather, he would confer with the plant physician, acquaint him with the nature of the employee-patient's condition, and leave it up to the plant physician to recommend and medically supervise his proper placement at work in the plant.

Such cooperation between the plant physician and the family physician can stem only from good communications between them and from adherence by both to the golden rule. Benefits would accrue therefrom to the employee-patient in the form of better and more prompt attention to his health needs; to the plant in the form of increased production attending the improvement of employee health and morale and decreased sick absence and turnover; and to the physicians involved in the form of enhancement of their diagnostic acumen and therapeutic skill.

Keeping Programs Within Limits.—Of course the millennium has not arrived, and physicians, being human, will err and may not always forgive.

Some plant physicians do perform and do permit their industrial dispensaries to perform ostensibly occupational health services outside of what are set as proper limits in this official A. M. A. policy statement and outside of the limits set by their state and county medical societies. The private practitioners, seeing this, cannot be blamed if they complain, even retaliate in various ways, such as by withholding that Utopian cooperation just discussed. Plant physicians so transgressing should admit it and should then forthrightly either restrict their occupational health activities within the limits accepted by their county medical society or present to the county medical society grounds in defense of such of these services as do exceed these limits and ask that the limits be extended to cover them. Suppose the society renders a decision unfavorable to the plant physician in this situation. He should abide by it. However, if he chooses not to abide by it, he should so declare, rather than pretend to abide by it and then not do so. If the plant physician in this situation has the courage of his conviction that he is right in including in his occupational health program these services disapproved by his county medical society, he should set about winning the society over to his way of thinking in as friendly a manner as possible, not truculently or defiantly. He should not simply "draw his cloak about him" and sever relations with the society, with hurt feelings or in a smoldering, "ulcerogenic" rage.

The plant physician who, whether openly or covertly, continues to carry on ostensibly occupational health services beyond the limits prescribed or agreed to by his county medical society should prepare himself to pay, and prepare his company to pay, the price thereof. This price could be lack of cooperation, if not outright passive or active opposition, on the part of his confreres in private practice. This would indirectly and eventually exert a detrimental effect on the health and morale of the employees of the plant and on its sick absence, turnover, and production. The gains netted in return for this price might prove illusory and not worth the price in the long run if, indeed, in the "short run."

Communications.—Perhaps more frequent than actual transgressions are imagined or rumored transgressions of plant physicians. Not infrequently a family physician, extrapolating and generalizing from what he has heard, possibly from a patient of his who works in a plant, jumps to the conclusion that the plant's physician and dispensary personnel are performing, under the guise of their occupational health program, services outside the limits set or accepted by the county medical society. Possibly he does not speak about the matter to the plant physician concerned, simply behaves toward him as though the allegations were established. Not being acquainted with such allegations, the plant physician has no opportunity to refute them and state what he is actually doing. The family physician in this situation should, in all fairness to the plant physician, tell him what he has heard about his occupational health service and invite his comments, explanation, and clarification.

The plant physician behaves, at times, equally unfairly toward the family physician. The allegation is likely to be false or exaggerated which the plant physician hears to the effect that the family physician is aiding and abetting abuse of sick leave by a plant employee, that he is speaking disparagingly of the plant's occupational health program, or that he is interfering with the plant physician's exercise of his prerogative to guide medically the placement of an employee returning to work after an illness or injury. The plant physician, on hearing such an allegation, should, in adherence to the golden rule, seek a man-to-man talk with the family physician, tell him what he has heard about him, and invite his comments, explanation, and clarification.

Most physicians serving industry do so on a part-time or on-call basis and carry on a private practice also. I might digress to say that the vast majority of the employed population in the United States work in establishments too small to have a medical department of their own and that such services as they receive of the preventive medical sort described here must be at the hands of physicians in private practice in the community. Many physicians serving industry on a part-time or on-call basis and also carrying on a private practice are suspected of attracting, and many undoubtedly do attract, employees of the plants they serve into their offices as private patients, in a manner both unethical and unfair to their confreres in private practice. This is difficult to avoid. However, every physician connected with industry who practices privately should "bend over backward" to avoid committing and avoid even appearing to commit this offense. Here, certainly, adherence to the golden rule is advisable.

There is another way in which the plant physician may offend the private physician. Suppose the latter is taking care of a plant employee, either for a nonoccupational condition or, under workmen's compensation, for an occupational condition. Suppose that the plant physician believes that the attending physician is not treating the patient correctly or that he is performing unnecessary surgery, unduly prolonging hospitalization, requiring too many house or office calls, or charging excessive fees. Suppose the plant physician expresses such opinions to the employee-patient or to the plant management. When the attending physician hears of this, as he sooner or later will, somehow, he is likely to be hostile to the plant physician. The plant physician, instead of, or at least before, speaking critically of the attending physician to the employee-patient or plant management, should talk the matter over with the physician himself.

Grievances.—Sometimes, however, two individuals will conceive a mutual distrust and will fail to try, or will be unable, to reach a reconciliation. They may even refuse to talk with each other. Likewise, an individual may embark on and persist in a course of action which he believes right but which some of his peers believe wrong. In all such situations, there should be an impartial third party to hear both sides and give them its findings and recommendations. The county medical society's grievance committee should so function. It should afford any plant physician or family physician whose actions or utterances, actual or alleged, have given rise to a misunderstanding or estrangement ample opportunity to give an account of such actions or utterances and to explain and justify them. It is hoped that this committee will have the wisdom and the courage to render a decision calculated to serve best the interests of all concerned and of medicine. It is hoped that the society will press for, and the physicians involved will go along with, the implementation of this decision.

Summary

There is now a well-defined area of medical practice designated industrial or occupational medicine. Physicians engaged in such practice should conscientiously try to avoid encroaching into the domain of the private practitioner, just as the latter should recognize the prerogatives of the industrial physician and should meet him halfway in his offer to communicate and cooperate.

The county medical society should charge one of its committees, such as its grievance committee, to hear and amicably resolve, to the satisfaction and in the best interest of all concerned and of medicine, (1) any complaint to the effect that an industrial physician has failed to keep his program within limits accepted by the medical society and (2) any complaint to the effect that a private physician has usurped an industrial physician's prerogative or otherwise unfairly and unwarrantedly interfered with his program.

A seminar meeting in occupational health, held annually in every state, could prove invaluable in promoting occupational health and in establishing and maintaining good professional relations between physicians engaged in such work and their confreres in private practice.

ANGIOCARDIOGRAPHY.—Angiocardiography has come of age. It is an established and valuable procedure in the hands of a competent team in the diagnosis of congenital malformations of the heart and great vessels. A resurgence in its use has come about through a perfection of the technics for selective angiocardiography and retrograde aortography together with a marked mechanical improvement in high-speed biplane serial radiographic equipment and the development of safer contrast media. Angiocardiographic examinations, by establishing preoperative diagnoses, have made it possible to determine whether hypothermia or extracorporeal circulation will be more suitable for a particular case. Further advances in cine-angiography with image-intensifying equipment and the better viewing afforded by the Spectroscope offer even greater possibilities for more effective use of this procedure.—W. G. Scott, M.D., and B. S. Loitman, M.D., Angiocardiography in Diagnosing Congenital Malformations of the Heart and the Great Vessels, *Postgraduate Medicine*, May, 1959.

FLOW SHEET FOR USE IN OBSTETRIC COAGULATION PROBLEMS

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Success in preventing and treating hemorrhage in obstetric patients depends on the development of a systematic procedure which precludes the possibility of omissions and oversights. The danger of coagulation defects must be kept constantly in mind. The plan here outlined includes four tests designed to reveal such defects. If any exist, blood must be obtained for typing and crossmatching in preparation for transfusions of whole blood. Three procedures are outlined for treating patients whose blood is deficient in fibrinogen, contains a heparin-like factor, or manifests fibrinolytic activity. The primary aims are early diagnosis and prompt treatment.

The problem of managing acute hemorrhage in the obstetric patient presents a challenge to every obstetrician. Proper diagnosis and adequate treatment demand an orderly and rapid sequence of procedures. Current reports in the literature stress the occurrence of coagulation defects in antepartum, intrapartum, and postpartum hemorrhage. The incidence of a coagulation defect has been found to be as high as 1 per 1,000 live births in a recent series.[1] It is the purpose of this communication to present a flow sheet which has been developed at the Los Angeles County Hospital for following the course of such patients. This record, shown in the figure and table, has been most helpful in the management of acute hemorrhage complicating pregnancy.

Diagnosis

Since the primary aims are early diagnosis and prompt treatment, the importance of a high index of suspicion cannot be overemphasized. The physician who infrequently practices obstetrics may be unfamiliar with some of the bedside procedures in the diagnosis and management of coagulation defects associated with pregnancy. These bedside procedures have been outlined in detail in previous articles.[2] In brief, they are the clot observation test, qualitative fibrinogen estimation, and the determination of circulating heparin-like factor or fibrinolysin level.

The clot observation test appears essential in all cases of suspected abruptio placentae, postpartum bleeding which does not respond to the usual pro-

Flow Sheet for Hemorrhage, Abruptio Placentae, Coagulation Defect, and Other Disorders (Reverse Side)

Clot Observation Test.—Five-milliliter sample of maternal blood, in 15-ml. test tube. Gently agitate four or five times. In our experience at this hospital the clotting mechanism is defective if there is no clot within six minutes or if a clot forms which is not solid and lyses within one hour. In other hospitals with other equipment the maximum normal time of clotting may be longer.

Size: After clot retraction a normal clot should occupy 35 to 45% of the total volume of the blood specimen.

Stability: Allow clot to stand one-half hour, then shake test tube a few times. A normal clot will withstand this procedure without breaking.

Bedside Qualitative Fibrinogen Estimation Based on Clot Observation Test.—Clotting time less than 6 minutes: fibrinogen level probably greater than 150 mg.%.

Clotting time more than 6 minutes, with poor clot: fibrinogen level probably 100 to 150 mg.%.

No clot in 30 minutes: fibrinogen level probably less than 100 mg.%.

Bedside Determination of Heparin-like Factor.—Five milliliters of unclotted maternal blood plus 5 ml. of normal control blood. Failure of the combined specimen to clot indicates the presence of a heparin-like factor.

Bedside Determination of Circulating Fibrinolysin.—Five milliliters of unclotted maternal blood plus 5 ml. of clotted normal control blood is held at room temperature. Lysis of the normal clot within one hour indicates the presence of fibrinolysin.

Fibrinogen Replacement.—Four grams of fibrinogen must be given at a rapid rate to the patient with little or no circulation fibrinogen, to elevate the serum fibrinogen above the critical level of 100 mg.%. If the clotting defect is not significantly improved within one hour, an additional 4 Gm. of fibrinogen should be given. Termination of the pregnancy should be expedited.

Treatment of Heparin-like Factor.—Dosage of protamine sulfate: 20 to 50 mg. intravenously. This should be given very slowly and should not be repeated unless persistence of the heparin-like factor can be subsequently demonstrated.

Treatment of Fibrinolysin.—Dosage of hydrocortisone: An initial intravenous dose of 200 mg. should be given, followed by 100 mg. every four hours during the first 24 hours. Following this the dose can be decreased 100 mg. per day, and the intramuscular route can be used.

Height of Fundus.—Measure with calipers in centimeters from symphysis pubis.

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cedures of uterine massage, oxytocics, and repair of lacerations, intrauterine fetal death, and profound shock suggestive of amniotic fluid embolism. In essence, the diagnosis of fibrinogen deficiency, heparin-like factor or fibrinolysis must be suspected in every case of hemorrhage of undetermined etiology.

Management

Once the diagnosis of a coagulation defect has been established, proper management must be instituted immediately. In the absence of a well-organized course of procedure, the most routine measures may be inadvertently overlooked. The steps which should be taken in rapid sequence are

DIAGNOSIS __________ Blood Group __________

Grava _____ Para _____ AB _____ SB _____ Weeks Gestation _____ Date __________

		1st Hour				2nd Hour				3rd Hour			
Time	am-pm	15 min.	30 min.	45 min.	60 min.	15 min.	30 min.	45 min.	60 min.	15 min.	30 min.	45 min.	60 min.
Blood Pressure													
Pulse													
Respirations													
Fetal Heart Tones													
*Height of Fundus													
Uterine Contractions													
Frequency													
Duration													
Intensity													
Cervix Dilation													
Effacement													
Membranes													
Station													
*Clotting Time													
Size													
Stability													
*Fibrinogen, Qualitative													
Quantitative													
*Heparin-like Factor													
*Fibrinolysin													
Est. Blood Loss													
Hemoglobin													
Hematocrit													
Blood Volume													
Intravenous Fluids													
–Whole Blood													
* –Fibrinogen													
–Plasma													
–Other													
Pitocin													
*Protamine Sulphate													
*Acth													
*Cortisone													
Urine Output													
Blood on Hand													
Fibrinogen on Hand													

Surname First Name Middle Name Age Race Hospital Number Ward

Flow sheet for hemorrhage, abruptio placentae, coagulation defect, and other disorders. (*See reverse side of sheet, presented in table.)

to (1) obtain blood for typing and crossmatching, (2) administer whole blood in amounts sufficient to replace the estimated blood loss, with general antishock measures, (3) give fibrinogen intravenously, when indicated, until the blood clot is stable, (4) institute antiheparin or antifibrinolysin therapy as indicated, and (5) expedite delivery.

Summary

The most important single point in the diagnosis of a coagulation defect in pregnancy is a high index of suspicion. A flow sheet has been found useful in the diagnosis and management of this problem.

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Printed copies of the flow sheet may be obtained from Cutter Laboratories, Berkeley 4, Calif.

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OBSERVATIONS ON ONE HUNDRED CASES OF CEREBRAL ANGIOMA

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In recent years there has been a revival of interest in the surgical treatment of cerebral angiomatous malformations.[1] In part, this is due to the widespread use of cerebral angiography which allows for more precise definition of this lesion in regard to size, location, and source of blood supply. In addition, the application of hypothermic and hypotensive techniques to neurosurgery has markedly reduced the hazards of uncontrolled hemorrhage during operation. Despite these advances, the operation is not without risk, as it may result in irreversible neurological deficit, such as aphasia, hemiplegia, or other focal neurological defects. It seems appropriate, therefore, that a review of the symptoms and natural history of this disease be undertaken to afford a background for assessing the value of operative intervention.

Various aspects of cerebral angiomas have appeared in the literature.[2] This report deals with the clinical, electroencephalographic, pneumographic, and roentgenographic findings. In a future communication, I shall report on the longevity of patients with such lesions, the natural history of the disease, and the comparative results of surgical and conservative treatment.

Cushing and Bailey[2a] divide all the cerebral vascular abnormalities into two groups: (1) the true neoplasms or hemangioblastomas and (2) the cerebral vascular malformations. The latter group, which is the subject of this paper, is divided into three forms: telangiectases, venous angiomas, and arterial angiomas (arteriovenous aneurysms).

Symptoms that should alert the clinician to consider diagnosis of cerebral angioma include focal convulsive seizures in patients under 30 years of age, evidence of subarachnoid hemorrhage, cranial bruit, linear streaks of calcification in x-ray films of the skull, and recurrent hemicrania. The patients in this series were proved to have a true angiomatous malformation by cerebral angiography, intracerebral operation, or autopsy. Of the 100 patients, 52 were females and 48 males.

These cerebral vascular malformations are assumed to result from defective development of the primitive vascular plexus.[3] Such angiomas may be very small and located on the surface of the brain. They may also be huge, in the form of a solid triangle with the base on the surface of the brain and the apex deep in the cerebrum near the ventricular system.

Case Material

The patients included in this study were proved to have a true angiomatous malformation by one of the following methods: cerebral angiography, intracerebral operation, or autopsy. Patients studied were admitted to either the Neurological Institute of New York or the American University Hospital in Beirut, Lebanon.

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Of the 100 patients studied, 52 were females and 48 males. Their ages ranged from 3 months to 63 years. The average age at which the first symptoms occurred was 28 years. The patients were evaluated for the following major clinical characteristics of the disease: convulsive seizures; subarachnoid hemorrhage, with or without focal neurological signs; headache; cranial bruit; linear calcification seen in x-ray films of the skull; electroencephalographic abnormalities; pneumoencephalographic abnormalities; changes in the cardiovascular dynamics; and abnormalities of the peripheral blood cell count.

Results

Convulsive Seizures.—Seventy patients suffered from convulsive seizures; 50 of them had focal seizures and 20 had generalized attacks without aura. The lesions in the patients who had generalized convulsions without aura were usually located in either the temporal or the frontal lobes. In almost all the 50 patients who suffered from focal seizures, the aura was of localizing value. In fact it was a more accurate index to the location of the lesion than the electroencephalographic study.

Forty-eight of the 70 patients who suffered from convulsive seizures received anticonvulsant medication regularly. In 25 patients the attacks were completely controlled; in 14 the seizures were reduced in frequency; and in 9 there was no change in the seizures. One patient developed attacks of status epilepticus after surgical removal of an angioma. The intravenous administration of thiopental (Pentothal) sodium was effective in controlling these attacks.

Hemorrhage.—Intracranial hemorrhage, the most serious complication of cerebral angiomas, occurred in 45 patients. Bleeding into the subarachnoid space was present in all 45 patients. In 21 patients there was simultaneous subarachnoid and intracerebral hemorrhage. Three patients had three episodes of hemorrhage, 21 had two, and 21 had only one.

Headaches.—Forty patients had recurrent headaches. Headaches which developed at the time of subarachnoid or intracerebral hemorrhage or after a convulsive seizure were excluded from this analysis. In 20 patients the headaches were preceded or accompanied by visual phenomena simulating those of migraine. Of the 20 who had migraine-like headaches, 5 suffered from diplopia during the attack of headache. Hemicrania, when present, was always on the side of the angioma.

Cranial Bruit.—Twenty-five of the 100 patients had an audible bruit. This was most commonly found over the eyeballs or mastoids. In five of the patients with an audible bruit, the arteriovenous malformation was fed by the external carotid artery.

Blood Pressure, Heart Size, and Heart Murmurs.—Ninety-nine patients had normal blood pressure. In one patient the pressure was 160/100 mm. Hg. Enlargement of the heart shadow in x-ray films of the chest was not found in any of the patients. This is in contrast to the report of Brock and Dyke,[4] who found enlargement of the heart in four of eight patients. Low diastolic pressures have been reported by Shenkin and associates.[5] This was present in one patient in the present series. None of the 100 patients had polycythemia.

X-rays of the Skull.—Intracerebral calcifications, in the form of circular or parallel streaks, were present in 20 patients. In four there was widening of the sella turcica and osteoporosis of the dorsum sellae. In 15 patients the vascular channels in the cranium overlying the arteriovenous aneurysm were enlarged.

Electroencephalographic Studies.—The electroencephalogram showed abnormal findings in 56 patients (to compare, see study by Groethuysen and associates [6]). Correct lateralization of the lesion was obtained in 42 patients, all of whom had convulsive seizures. In the remaining 14 there were no focal abnormalities. Of the 21 patients who had intracerebral hemorrhage, 18 developed convulsive seizures, and all of these had electroencephalographic changes on the side of the lesion.

Pneumographic Studies. — Pneumoencephalography or ventriculography was performed in 28 cases because the symptoms and signs suggested an expanding intracranial mass. Reports in the literature indicate that the usual finding in the pneumoencephalogram is localized or generalized atrophy of one hemisphere. Occasionally, there is shifting of the intracranial contents plus atrophy of the brain of the side of the shifted ventricle.[21] Fifteen of the patients in the present study, however, showed pneumoencephalographic changes characteristic of an expanding mass without atrophy. Angiography was performed in four of these patients, and the arteriovenous aneurysm was, of course, clearly demonstrated. The other 11 patients were subjected to craniotomy, with the preoperative diagnosis of brain tumor. Eleven patients showed local atrophy at the site of the arteriovenous aneurysm. Two showed generalized atrophy of the cerebrum and cerebellum; these two patients had large arteriovenous aneurysms. The malformation apparently produced a large shunt, and the atrophy of the cerebrum and cerebellum was explained on basis of decreased blood supply to these areas of the brain.

Summary and Conclusions

In 100 patients suffering from cerebral angioma, the lesion was confirmed by angiography, operation, or autopsy. The onset of symptoms was in the third decade of life in the majority of cases. Symptoms indicative of intracerebral hemorrhage occurred in 45 patients.

Twenty patients suffered from migraine-like headaches. The headache, when hemicranial, was always on the side of the lesion. Convulsive seizures occurred in 70 patients. These were focal in nature in 50. The aura was of more value in localization of the lesion than the electroencephalogram. About two-thirds of the patients suffering from seizures responded well to anticonvulsant medication. Twenty-five of the patients had an audible bruit.

None of the patients had polycythemia, enlargement of the heart, or cardiac murmurs. Only one patient had a low diastolic pressure.

The electroencephalogram was useful in lateralization of the lesion in the 42 patients who suffered from focal seizures. Linear streaks of calcification were present in the x-ray films of the skull in 20 patients. Findings indicative of expanding intracranial lesions were present in the pneumoencephalograms of 15 patients, and focal or generalized cortical atrophy was present in 11. The lesion was clearly demonstrated by angiography in all patients in whom these tests were performed.

The following group of symptoms should alert the clinician to consider the diagnosis of a cerebral angioma: recurrent hemicrania, always localized to one side of the head; the occurrence of focal convulsive seizures in patients under 30 years of age; evidence of subarachnoid hemorrhage, with or without focal neurological signs; cranial bruit; and linear streaks of calcification in the x-ray films of the skull. The diagnosis can be confirmed by angiography.

Professors H. Houston Merritt and J. Lawrence Pool and colleagues at the American University Hospital of Beirut gave permission to use case records of their patients. Dr. Melvin D. Yahr, Neurological Institute of New York, aided in study of these cases.

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WHO CAN TRAVEL SAFELY BY JET PLANE?—Air travel per se, and particularly jet air travel, does not present a hazard to patients who are transportable. However, owing to a lack of medical facilities and trained medical personnel aboard commercial aircraft and in consideration of the comfort of fellow passengers, certain restrictions are necessary:

A patient whose illness is objectionable to other passengers because of appearance or odor should not be permitted to travel on commercial aircraft. Patients with contagious diseases should not be carried for obvious reasons. A patient who, because of his illness, cannot take care of his needs should not be carried unless, by previous arrangements, a suitable medical attendant travels with him. Cabin attendants are usually too busy with routine duties to provide anything but simple emergency first aid care to an individual passenger. Patients whose behavior might be upsetting or hazardous to fellow passengers should not be carried. This applies primarily to patients with severe emotional disturbances. Patients with illness of a type or severity to present a serious hazard in a mild respiratory stress situation when expert medical care is not immediately available should not fly on commercial aircraft. Illnesses associated with trapped gases in body cavities, such as pneumothorax, should not fly because of gas expansion at altitude.

Problem cases should be evaluated for flight by the private physician on an individual basis. As an example, since there are no adequate facilities to perform a delivery in the air, a woman beyond the eighth month of pregnancy should not fly. Air travel is not injurious to an expectant mother or the unborn child, but a delivery in anything but medical environment can cause unnecessary problems. . . .

Airline medical directors are available for consultation, with the personal physician, on cases presenting special or difficult problems in relation to air travel.—M. Frederick Leeds, M.D., Medical Aspects of Commercial Jet Air Travel, *California Medicine,* April, 1959.

STEROID TREATMENT OF LYE BURNS OF THE ESOPHAGUS

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The effectiveness of cortisone in preventing esophageal stenosis after ingestion of lye in rabbits suggested the use of steroids for the prevention of stenosis in children who have swallowed lye. Prednisone was administered to 13 children who had swallowed lye. The data are summarized. In three cases which are described in detail the lye was strong enough to cause visible lesions in the mouth. The dosage of prednisone was 10 mg. each six or eight hours for periods up to 16 days, with tetracycline to prevent infection. Neither infection nor stricture appeared in any of the 13 children. Although the treatment with steroids appeared to be effective, the real answer lies in the prevention of accidents with lye.

The frequent ingestion by children of substances containing lye and the frequent occurrence of esophageal strictures and stenosis as a result make the treatment of this ingestion important. The addition of steroid therapy to the management of this problem has greatly altered the prognosis, and for this reason we wish to present our results with 13 children so treated.

A survey in 1957 showed lye to be the fifth leading cause of poisoning in patients under the age of 19 years.[1] It is mentioned especially frequently as an important problem in the 1-to-4-year age group. Prior to the introduction of steroids, it was estimated by various authors that from 56 to 70% of those ingesting lye developed esophageal strictures.[2] Hanckel,[3] in 1951, described the pathological physiology which occurs. The immediate reaction is one of inflammation and edema, causing dysphagia which disappears in two or three days as the swelling subsides. This is followed by a period of normal swallowing until scar tissue gradually forms, and obstruction of the esophagus occurs in two to three weeks after the initial burn. Difficulty in swallowing solids appears first, then difficulty in swallowing liquids, with complete stenosis in 50 to 60% of cases. Untreated, all of these patients will die from dehydration and starvation. Treatment until recently has consisted of bougienage, either blind or visually with the aid of an esophagoscope, or surgical resection. A 25-year survey done in 1956 encompassed cases of 233 patients; 206 had severe esophagitis, 188 responded to repeated bougienage, 14 required resection, and 5 died from perforation of the esophagus.[2b]

Rosenberg and associates,[4] in 1951, undertook the use of cortisone in experimentally produced sodium hydroxide burns of the esophagus in rabbits and found that, while 7 of 8 controls developed severe strictures, only 1 of 17 treated with cortisone developed a mild stricture. However, 10 of the 17 died of infection, predominantly mediastinitis. In a repeat study,[5] in 1953, the same group added penicillin to the treatment and found that only 3 of 21 rabbits so treated died (2 from diarrhea, 1 from pneumonia) and only 1 developed a stricture.

Weisskopf,[6] in 1952, treated a 17-month-old boy who ingested lye with cortisone and oxytetracycline (Terramycin) therapy with a good result. He then produced lye burns in seven dogs which he treated with cortisone and oxytetracycline for from 7 to 120 days. No strictures resulted, but one died from pneumonia; strictures developed in seven of eight controls. This work prompted the use of steroids in children who accidentally ingested lye-containing products. The first report of any magnitude was that of Ray and Morgan,[7] in 1956, who reported 10 patients treated with cortisone and antibiotics in whom no strictures developed and one patient in whom treatment was begun four days after ingestion and in whom a stricture developed after three months. Cleveland and associates,[8] in 1958, reported a similar program, with slightly less good results. Three of 14 whom they treated developed strictures, and 2 of 4 who had less than optimum treatment also developed strictures.

We have been using steroids and antibiotics in the treatment of lye ingestion for over two years. Since our results to date have been uniformly good, we wish to outline the regimen used and comment somewhat about it.

Treatment and Results

A total of 13 children have been treated with prednisone (Meticorten) and antibiotics, all but one in the past two years. At the beginning the dosage schedule was not definitely established, and there was some variation in the length of treatment, depending on the judgment of the attending staff, severity of the burn, and findings at esophagoscopy. However, for the past year the procedure

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has been standardized, and the last 11 patients were treated similarly, with the exception of the patient in case 7, who ingested a preparation containing only 4.5% sodium hydroxide and who did not have esophagoscopy. The other 12 patients ingested a concentrated sodium hydroxide preparation.

On admission all patients had a nasogastric tube inserted for feeding purposes, which was removed after three days. Two patients pulled out their tubes within 24 hours, and they were not reinserted. Clear liquids, progressing to a soft diet in three days, were given. A chest x-ray and tuberculin test were done on the day of admission, and therapy with prednisone was started with approximately 1 mg. per pound of body weight per 24 hours, divided into three or four daily oral doses. Tetracycline was given in a dosage of 15 to 20 mg. per pound per day orally. Esophagoscopy was done 7 to 10 days after admission; if no burn was noted, treatment with steroids was tapered off over the next few days, and tetracycline was withdrawn one day after steroid therapy was discontinued. If a burn was found in the esophagus, therapy with prednisone was continued for another week and a "barium swallow" performed. If no stricture was noted on the "barium swallow" (and none was), treatment with prednisone was then tapered off at a slower rate over the next two to three weeks and stopped. Blood pressures were checked daily and frequent urinalyses for sugar were performed; no complications were noted. No supplemental potassium was given, and there was no restriction of salt intake.

*Data on Thirteen Patients Treated for Lye Burns of the Esophagus**

Case	Age, Mo.	Days of Intensive Prednisone Dosage	Esophagoscopy Results	Follow-up, Mo.
1..............	18	6	Not done	42
2..............	36	9	Not done	24
3..............	14	13	Hyperemia and edema	12
4..............	8	12	Hyperemia	12
5..............	30	13	Hyperemia and ulceration	12
6..............	30	10	Hyperemia and edema	11
7..............	20	6	Not done	8
8..............	36	15	Hyperemia and edema	5
9..............	36	13	Hyperemia	4
10..............	24	14	Hyperemia and edema	3
11..............	30	16	Granulations and bleeding	3
12..............	24	10	Normal	2
13..............	18	16	Hyperemia and edema	1

* Results of "barium swallow" were normal in all cases except 1 and 7, in which cases study was not done.

There were no strictures in any of the 13 patients so treated, and there were no complicating infections. All children were asymptomatic within three days after admission and remained so. Esophagoscopy was performed in all but the first two patients and the seventh, who ingested a dilute lye preparation. In all but one there was evidence of burn in the esophagus, either hyperemia and edema or ulceration. A "barium swallow" was performed in 11 patients at about two to three weeks after ingestion and was normal in each instance. Follow-up varied from one month to three and one-half years, and no subsequent strictures have developed. A summary of the cases is presented in the accompanying table. Three representative cases are described in more detail.

Report of Cases

CASE 3.—A 14-month-old girl was admitted to the Delaware Hospital on Dec. 20, 1957, with a history of having ingested an unknown amount of a concentrated lye preparation just prior to admission. Physical examination revealed a well-developed child, weighing 18 lb. (8,164 Gm.), and in no apparent distress. Her lips were swollen, and burns were seen in the inside of her mouth, with partial denudation of her tongue. No other abnormalities were noted. Routine blood cell count revealed a hemoglobin level of 9.3 Gm. per 100 cc. and a hematocrit of 33%; white blood cell count and differential were within normal limits, as was the urinalysis. A tuberculin test was negative, and her chest x-ray was reported as showing normal heart and lungs. A nasogastric tube was passed immediately after admission, and through it she was fed a diet of food prepared in a "blendor" until Dec. 28, when it was removed and a soft diet given. She was given therapy with prednisone, 15 mg. for the first dose and then 10 mg. every eight hours, and tetracycline, 150 mg. for the first dose and then 100 mg. every eight hours. On Dec. 28 esophagoscopy was carried out with the patient under general anesthesia, and marked hyperemia and edema were seen in the proximal portion of the esophagus and also in its distal portion. Prednisone therapy was continued in the same dosage until Jan. 2, 1958, after which it was reduced stepwise over the next week and withdrawn on Jan. 8. Tetracycline therapy was continued until three days after her discharge on Jan. 8. A "barium swallow" was performed on the day of discharge and was normal. The child has been asymptomatic for over a year.

CASE 10.—A 24-month-old girl was admitted to the Delaware Hospital on Dec. 2, 1958, with a history of ingestion of an unknown quantity of a concentrated lye preparation about 45 minutes prior to admission. She vomited immediately after swallowing the lye. Initial physical examination revealed a well-developed child, weighing 28 lb. (12.7 kg.), and in no apparent distress. Her tongue was desquamated over an area of about 1 in. in diameter; no other evidence of burn was noted, and the remainder of her examination was within normal limits. Blood cell count was normal; urinalysis revealed 1+ albumin, 4+ acetone, and 8-10 white blood cells per high-power field on admission, but was normal when repeated. A tuberculin test was negative, and a chest x-ray was reported as showing normal heart and lungs. A nasogastric tube was inserted on admission and a full liquid diet was begun; however, she pulled out her tube after about 36 hours and it was not reinserted. She tolerated orally given fluids well, and she was given a soft diet on Dec. 5. Prednisone, 10 mg., and tetracycline, 125 mg., were given every six hours. On Dec. 12 esophagoscopy was carried out with the patient under general anesthesia, and the esophagus appeared normal. The dosage of prednisone was then tapered off over the next week. She was discharged on Dec. 19, still on therapy with 5 mg. of prednisone every eight hours, and this was reduced gradually and stopped on Jan. 7, 1959, at which time the tetracycline therapy was also discontinued. She has had no symptoms since.

CASE 13.—An 18-month-old boy was admitted to the Delaware Hospital on Jan. 7, 1959, with a history of ingestion of a concentrated lye preparation from a bottle approximately two hours prior to admission. He vomited immediately after the ingestion. Physical examination revealed a well-developed boy, weighing 27 lb. (12.2 kg.), and in no apparent distress. Denuded areas were present on his lips, gums, tongue, and posterior pharynx, but no other abnormalities were noted. On admission, blood cell count and urinalysis were within normal limits; tuberculin tests were negative; and a chest x-ray was reported as showing normal heart and lungs. A nasogastric tube was inserted on admission, through which a full liquid diet was given for three days. At the end of this time the tube was removed and a soft diet given, which he tolerated well. Prednisone, 10 mg. every eight hours, and tetracycline, 100 mg. every six hours, were given. On Jan. 16 esophagoscopy was carried out with the patient under general anesthesia and two areas of hyperemia and edema were noted—one at about the level of the arch of the aorta and one at the level of the diaphragm. Therapy with prednisone was continued until Jan. 23, after which the dosage was tapered gradually and discontinued on Feb. 2, at which time the tetracycline therapy was also stopped. A "barium swallow" was performed on Jan. 27 and was normal. The child was discharged on Feb. 2, 1959, and has remained asymptomatic.

Comment

While the optimum dosage schedule and the length of treatment is yet to be definitely determined, we feel that our regimen as outlined is quite adequate. Although most of our patients showed signs of adrenal cortical hyperfunction, we have had no serious complications. It was originally felt that tube feedings should be given for the first three days, the period of initial inflammation and edema; but we are now wondering whether there might not be less trauma associated with swallowing clear liquids than with the continued irritation of a foreign body such as a nasogastric tube. Passing the tube initially is also not without danger, and, despite the fact that we have had no difficulty so far, we are contemplating the elimination of the tube in our treatment. Swallowing a string has been suggested,[7] but since there is little likelihood of complete esophageal stenosis in patients treated adequately with cortisone, this is probably also an unnecessary procedure. Our two patients who removed their tubes before the initial three days passed swallowed clear liquids easily, and we have given sips of liquids to others, while their tubes were in place, with no difficulty. All patients have tolerated a soft diet well after the third day, and this should be continued until after three weeks, when a general diet can be given.

Despite the fact that the more severe consequences of lye ingestion can be averted with proper and early treatment in most cases, it is still a serious problem. The real answer lies in the field of prevention, especially through dissemination to the public of information about the dangers inherent in leaving poisonous substances within the reach of children.

Summary

Stricture of the esophagus after the ingestion of lye can be prevented in most instances. In the past two years we have found treatment with steroids and antibiotics to be successful in 13 children who ingested lye.

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SIMPLE PAPER TEST FOR DETERMINING BACTERIAL SENSITIVITY TO ANTIBIOTICS

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The test paper here described makes it relatively easy to choose the antibiotic best suited for treatment of a given bacterial infection. Each type of test paper bears both a culture medium and an antibiotic and is supplied, dry and sterile, in a transparent envelope. For a given test, the paper is wetted and inoculated and the envelope with its contents is incubated. It is not necessary to wait for the appearance of visible colonies because the metabolic activity of the bacteria is detected by an indicator (triphenyltetrazolium chloride) which is colorless until reduced to a bright red dye by bacterial enzymes. The reliability of the new test was established by a comparative study with other methods in 100 clinical cases. The test paper is easily stored, and the entire unit can be incinerated after use. It is therefore useful in general office practice and should help to make sure that each patient receives the most effective antibiotic.

Since the advent of antibiotics concerted effort has been made to devise tests for determining microbial susceptibility to specific antibiotics which could be used by clinicians as a reliable guide in selecting the most effective antibiotic for use in bacterial infections. Although the tube dilution and agar plate–antibiotic disk techniques have become standard tests in hospital laboratories, they have not been widely used in the physician's office. There are many reasons for clinicians not adopting these techniques in office practice, but probably the most important are that the tests are too cumbersome, time-consuming, and relatively expensive.

The object of this investigation was to develop a colorimetric paper test which would be easy to read, accurate, convenient, and stable. If these criteria were met the test could be used routinely in office practice, where the majority of patients with infections are treated.

It became apparent that to achieve these objectives the test paper would have to incorporate all ingredients necessary for all sensitivity testing, that is, both the culture medium and the antibiotics. In addition, since visualization of bacteria on paper is impossible, the test paper would also have to contain an indicator of bacterial activity or growth. Many indicator systems[1] were studied but only the indicator triphenyltetrazolium chloride was found satisfactory. This indicator is colorless in its oxidized form and bright red in its reduced form. It is reduced to the red triphenylformazan by a large number of bacterial enzymes. Under the conditions employed in the test, all bacteria reduced the indicator to a bright red color.

Schleicher and Schuell no. 470 filter paper was impregnated with tryptose phosphate broth containing 0.01% triphenyltetrazolium chloride. The paper was dried at 50 C. Numerous designs of filter paper were tested and found to be satisfactory but no unique advantage could be attributed to any of the designs. The test paper design shown in the figure seemed to provide zones of bacterial inhibition which could be read with maximum ease and clarity. The various antibiotics were pipetted onto the tips of the projections. After inoculation and incubation all areas where bacterial growth occurred were bright red. Areas in which inhibition occurred remained white.

The amount of antibiotic used on the projections was determined in two ways. First the concentration of antibiotic in micrograms per milliliter was determined by calculating the volume of hydrated medium contained in each projection. This determination was used in adjusting the concentration of antibiotics to correspond to the blood level of the antibiotic attainable. Then the test was compared with tube dilution studies on 43 different organisms. Some of the results of this study are shown in table 1.

The procedure used with the test papers was quite simple. After removal from a sealed plastic sack with sterile forceps the test paper was moistened by floating it on the surface of tap water for a few seconds. The test paper was then returned to the plastic sack and the surface of the paper swabbed with the infectious material. Scotch tape was used to seal the cut edge of the plastic sack and the unit was then incubated at 37 C.

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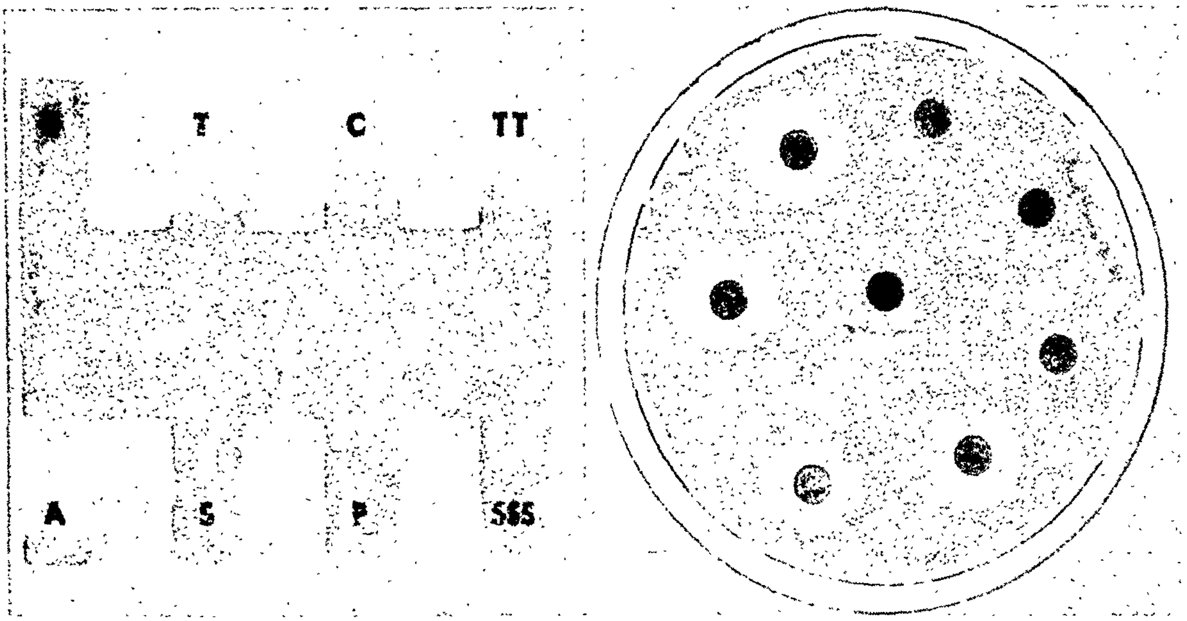
Although the use of tap water in the procedure would seem to destroy the validity of the test, it was found in sterility studies with 200 uninoculated test papers that only 6 of them became contaminated from use of the above procedure. The contamination occurred on the back of the test paper and consequently would not have interfered with the results, since readings are made on the front or printed side. The time required for completion of the test was found to depend on the number of organisms in the specimen used for inoculation. In the studies presented here all tests were completed in from 3 to 12 hours.

Clinical Studies

The clinical application of the paper culture test was studied in 100 unselected frank or suspected bacterial infections encountered in normal office practice (table 2). In 15 of the 100 cases the disk-agar test was run simultaneously. Infections in patients from whom cultures were made included boils, tonsillitis, abscesses, pharyngitis, sinusitis, infectious enteritis, urinary tract infections, felons, otitis, and folliculitis. In 76 cases antibiotic therapy was initiated empirically according to clinical judgment and experience before the results of the sensitivity test were available. Medication in the remaining 24 cases was initiated 12 to 24 hours later after completion of the culture tests. The degree of clinical change in the patient's condition was recorded after 24 and 48 hours. Response was judged excellent if there was marked improvement in 48 hours and the infection cleared later on therapy with the same antibiotic; good if there was moderate improvement in 48 hours and the infection cleared later on therapy with the same antibiotic; fair if there was only slight improvement and treatment with a different antibiotic was required to clear the infection; and poor if there was no improvement.

Of the 100 cultures 10% showed no growth. Of the 10 one was an aseptic sebaceous cyst; 2 were taken from patients previously on antibiotic therapy; 4 were from patients with a complaint of sore throat with only slight injection, and may have been viral; and 3 were urine cultures for suspected cystitis or pyelitis.

In the 15 cases where both test paper and disk-agar methods were employed the two methods were found to correlate qualitatively. In all cases the test paper could be read earlier than the agar plate and was found to be easier to interpret.



Comparison of *left,* test paper, and *right,* disk-agar methods for determining antibiotic sensitivity of bacteria. SSS—triple sulfonamide, C—chloramphenicol, E—erythromycin, S—streptomycin, A—chlortetracycline, T—oxytetracycline, TT—tetracycline, and P—penicillin.

Of the 76 patients given initial immediate medication only 23 (30%) showed sufficient clinical improvement within two days to warrant continuation of the first antibiotic. Of the 76 patients 53 (70%) required change to therapy with the antibiotics indicated by the test paper. All 10 of the sterile cultures were found in the 24 patients in whom the antibiotic was withheld, and the remaining 14 (18%) showed excellent to good clinical results on therapy with the antibiotics indicated by the test paper.

It is possible that the excellent results obtained by changing to the antibiotic indicated by the test paper cultures may have been due in part to the initial antibiotic used for from 24 to 48 hours. This was probably not the case, however, since the cultures showed little or no inhibition to those initial antibiotics prescribed at the same time that the culture was started.

Comment

Although bacterial growth takes place as well on blood agar as on the test paper, the paper test may be interpreted much earlier than the disk-agar technique because the result depends on bacterial enzymatic activity effecting a chemical color change rather than on the development of visible colonial growth. Zones of inhibition are more apparent on the test paper, especially in the case of streptococci and pneumococci where the extremely small colonies frequently make the reading of the disk-agar test difficult. Since the test paper is stored in dehydrated form there is no spoilage of the medium or deterioration of the antibiotics, and refrigeration is not required.

TABLE 1.—*Comparison of Tube Dilution, Disk-Agar, and Test Paper Methods for Determining Bacterial Sensitivity to Antibiotics*

		Antibiotic							
	Organism*	Triple Sulfonamide	Chloramphenicol	Erythromycin	Streptomycin	Chlortetracycline	Oxytetracycline	Tetracycline	Penicillin
Tube, µg/ml.	00	Resistant	4-8	0.02-0 05	Resistant	0.5-1.0	0.5-4.0	1-8 .	0.5-1.0
Agar disk		Resistant	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Paper test		Resistant	Sensitive	Sensitive	Resistant	Sensitive	Sensitive	Sensitive	Sensitive
Tube, µg/ml.	B-1	1-2	1-2	0.02-0.05	5-10	0.5-1.0	0.5-2.0	0.5-1.0	0.01-0.05
Agar disk		Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Paper test		Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Tube, µg/ml.	B-2	2.0-4.0	0.5-1.0	0.02-0.05	Resistant	0.1-0.5	1-2	2-4	0.01-0 05
Agar disk		Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Paper test		Sensitive	Sensitive	Sensitive	Resistant	Sensitive	Sensitive	Sensitive	Sensitive
Tube, µg/ml.	S-1	250-500	4-8	0.1-0.4	Resistant	0.1-0.4	1-2	2-4	0.01-0.05
Agar disk		Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive
Paper test		Resistant	Sensitive	Sensitive	Resistant	Sensitive	Sensitive	Sensitive	Sensitive
Tube, µg/ml.	E-3	Resistant	1-2	Resistant	Resistant	1-2	4-8	0.5-1.0	Resistant
Agar disk		Sensitive	Sensitive	Resistant	Sensitive	Sensitive	Sensitive	Sensitive	Resistant
Paper test		Resistant	Sensitive	Resistant	Resistant	Sensitive	Sensitive	Sensitive	Resistant

* 00=gram-positive nonhemolytic staphylococci; B-1=beta-hemolytic streptococci; B-2=hemolytic streptococci; S-1=hemolytic staphylococci; E-3=gram-negative rod coliform bacteria.

TABLE 2.—*Results of Clinical Application of Paper Test of Bacterial Sensitivity to Antibiotics in 100 Patients*

Results	Antibiotic Used Empirically	Antibiotic Changed After Culture on Fair-Poor Group	Antibiotic Withheld Until After Culture Report
Excellent	16	40	13
Good	7	11	1
Fair	31	1*	...
Poor	22	1*	...
Total	76	53	14

* Severe folliculitis responding to third antibiotic to which test indicated best sensitivity. These antibiotics were purposely not started second because they required intramuscular injection once or twice daily.

By clinical trials the test paper was found to be easy to use and reliable. As evidenced by the results in the series of patients studied it appears there is an absolute necessity for sensitivity testing in a surprisingly high percentage of infections seen in office practice. It seems clear that a large number of patients treated empirically with antibiotics do not receive the most effective antibiotic and have an unnecessarily prolonged course of illness. In addition, 10 of the patients in these tests were spared the hazards and expense of antibiotic therapy because of their sterile cultures.

Summary

A new paper test for determining microbial susceptibility to antibiotics was found to have the following advantages: The test is accurate as indicated by comparison with tube dilution and agar plate–antibiotic disk studies. It is simplified so that both medium and antibiotics are contained in one test. No refrigeration is required, because both the medium and the antibiotics are stable. The paper test is easier to interpret than the disk-agar test. Since the test is conducted in a sealed plastic sack there is no odor or danger of contamination, and the entire unit can be incinerated after completion of the test. Clinical studies have been done on 100 patients with the new test; these investigations indicate that a marked improvement in antibiotic therapy is obtained when the test is used together with clinical experience and judgment.

Previously it has been impractical to run routine sensitivity tests in office practice, but this new test paper should provide an extremely useful guide to antibiotic therapy for general office practice.

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METHYLPREDNISOLONE (MEDROL) IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

ANALYSIS OF RESULTS IN FORTY CASES

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Forty patients with active systemic lupus erythematosus were treated with methylprednisolone. Their ages ranged from 11 to 73 years. The pattern of clinical improvement was similar to that previously seen after the use of prednisone, triamcinolone, and other anti-inflammatory hormones; the fever abated in 24 hours, joint pains disappeared in several days, and pleural effusion and cutaneous lesions subsided in one to several weeks. The doses needed were of the same order of magnitude as those of prednisone and triamcinolone; the mean initial dose was 29.2 and the mean maintenance dose 25.9 mg. per day. While methylprednisolone seemed to differ from the other steroids with respect to some side-effects, the incidence of moonface, hirsutism, acne, and striae was about the same.

Over the past nine years, 325 patients with various forms of systemic lupus erythematosus have been treated with reassurance and rest and, when necessary, salicylates, antimalarials, and steroids.[1] For the last 16 months of this period, 40 patients who required steroid therapy were given a new synthetic, unsaturated, anti-inflammatory hormone: methylprednisolone (Medrol). The purpose of this report is to review experiences with this new agent and compare its results with those of triamcinolone, prednisone, and prednisolone.

Diagnosis and Treatment

Systemic lupus erythematosus is a chronic, multisystemic disorder with many diverse manifestations.[1d] Any system may initially be affected and heal, and patients are subject to many remissions and exacerbations. A thorough history must, therefore, be obtained, and when a patient has, for example, atypical rheumatoid arthritis [2] with pleural effusion, unusual skin lesions, and renal involvement, systemic lupus erythematosus must be considered.

In 80% of typical clinical cases, the diagnosis can be confirmed after repeated testing by finding L. E. cells, which are probably pathognomonic of the disease. A few L. E. cells have been found by myself and others in about 5% or more of patients apparently having rheumatoid arthritis.[3] Prolonged observation will be necessary to determine whether these cases will not terminate, as have similar ones, in overt systemic lupus erythematosus confirmed at autopsy. If cutaneous lesions are present, skin biopsy may confirm the diagnosis in another 10%, and diagnosis in the final 10% often rests on clinical data alone.

Treatment depends on the clinical severity of the illness. Antimalarial therapy is given if salicylates and rest fail or if cutaneous lesions are present; when these measures are inadequate or if the patient is critically ill or has neurological or renal involvement, steroid treatment should be started.

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Often, larger than expected amounts of the newer synthetic unsaturated steroids (prednisone, prednisolone, triamcinolone, and methylprednisolone) must be used to control exacerbations of the disease, since these hormones are not as predictable in their effects as are the older corticosteroids, such as cortisone and hydrocortisone. In the milder cases, the estimated amount of steroids is merely added to the therapeutic regimen of the patient. Often this means supplementing the medication of a patient with moderately well-controlled disease who is taking salicylates and antimalarials with small doses of these hormones. Periods of several days to a week or more are permitted to lapse between dosage changes in the milder cases. The increments used here are small, perhaps a 10 to 20% rise at weekly intervals until symptomatic and laboratory improvement is noted.

Table 1.—*Clinical Data on Forty Patients with Systemic Lupus Erythematosus Treated with Methylprednisolone*

	Range	Median	Mean
Age, yr.	11-73	40.0	37.5
Duration of disease, mo.	1-286	72.0	90.2
Duration of all steroid treatment, including methylprednisolone, mo.	1-92	17.5	25.9
Duration of methylprednisolone therapy, mo.*	1-15	4.0	5.0
Dosage, mg. per day			
Initial (21 cases)	8-96	16.0	20.2
Maintenance (40 cases)	6-144	16.0	25.9
Methylprednisolone ratio†			
Prednisone (8 cases)	0.75-1.25	1.1	1.1
Triamcinolone (4 cases)	0.5-1.0	0.9	0.8
Hydrocortisone (3 cases)	2.5-4.2	4.0	3.6
Prednisolone (2 cases)	0.83	0.8	0.8
Cortisone (1 case)	4.2	4.0	...

* Total patient months, 211.

† Methylprednisolone ratio = amount of drug required to produce equal anti-inflammatory effects on milligram for milligram basis, determined by dividing amount of methylprednisolone required for maintenance into amount of older steroids. To ascertain dosage of methylprednisolone to use in transfer, divide therapeutic ratio into 1: for example, with prednisone the therapeutic ratio is 1.1 and the factor is 1 ÷ 1.1 = 0.91 (91%) of the dose of prednisone.

In the severely ill patient, salicylates and antimalarials are not given early in therapy but the patient is immediately placed on therapy with large doses of steroids, such as 400 mg. per day of cortisone. This is done at the beginning in order to reverse rapidly the pathological process before irreversible damage is done. If no response occurs, the dosage of steroid is increased by 25 to 100%, depending on the situation, until improvement is noted. It is advisable to continue giving high dosages of steroids until all abnormal physical findings subside. Advanced renal disease, however, will not be benefited by continued large amounts of these hormones. If there is no change in the renal lesions after two months of adequate therapy, other treatments, such as that with nitrogen mustard, must be considered.[1a]

The clinical picture and hemoglobin level are used as the major guides to steroid therapy. When these normalize, the dosage is reduced slowly, with waiting periods for signs of relapse. More detailed information concerning treatment has been recently published.[1a]

Clinical Material

Forty patients with active systemic lupus erythematosus have been treated with methylprednisolone. The diagnosis was confirmed by findings of L. E. cells in 32 (80%) of the group, positive results of skin biopsy in 6 (15%), and a classic clinical picture in 2 (5%). None of the patients merely had rheumatoid arthritis with a few L. E. cells and no multisystemic disease. There were 30 females (75%) and 10 males (25%). Clinical data on these patients are given in table 1.

Thirty-one patients were receiving salicylate therapy to the point of mild salicylism with their steroids, and 15 were concurrently receiving antimalarial therapy. Ulcer diets and anticholinergics were given to only four patients who had a previous ulcer history and to one patient with an elevated 24-hour uropepsin level before steroid treatment. Sodium restriction was used in only four patients with edema due to nephropathy. Supplementary potassium was given to only one person who was vomiting excessively.

Dosage of Methylprednisolone.—In 21 patients, steroid therapy was initiated with methylprednisolone in a dosage ranging from the addition of 8 mg. per day to the therapeutic regimen of four patients who were on salicylate and antimalarial therapy to 96 mg. per day in a critically ill patient with acute pericarditis, bilateral pleural effusions, and anemia. In the other 19 cases, the patients' conditions had been stabilized on therapy with other steroids and they were then transferred to methylprednisolone therapy (table 1). Two patients were transferred from methylprednisolone therapy to that with other steroids; one, because of a lack of effect of 120 mg. per day, was changed to prednisolone therapy, 120 mg. per day. Subsequently the dosage of the latter steroid was increased to 200 mg. per day without any clinical improvement. The patient died two months later of pulmonary nocardiosis. The other patient was transferred from methylprednisolone to hydrocortisone therapy because of equivocal muscle weakness. This patient subsequently was given methylprednisolone therapy again and has had no further difficulty with it during the nine months prior to the time of writing. The steroid was given in three or four divided doses daily with meals.

Eight patients whose conditions had been stabilized on prednisone therapy were changed to that with methylprednisolone. The new steroid was 1.1 times more potent than prednisone, a methylprednisolone ratio of 1.1. This was determined by dividing the dose of prednisone needed for maintenance by the dose of methylprednisolone required for identical clinical effects. Table 1 lists the ratios of methylprednisolone compared to the older steroids for equal maintenance. The range of methylprednisolone varied between 0.75 to 1.25 times as potent as prednisone. In order to ascertain the amount of methylprednisolone required to change a patient from prednisone therapy to treatment with the new steroid, it is necessary to divide the methylprednisolone ratio into 1, i. e., $1 \div 1.1 = 0.91$; in other words, 91% of the dose of prednisone will be required.

Four patients were transferred from triamcinolone therapy to that with the new steroid. The median methylprednisolone ratio was 0.9 and the mean 0.8. Methylprednisolone was approximately 10 to 20% less potent on a milligram for milligram basis than triamcinoline. Three patients were transferred from hydrocortisone therapy to that with the new steroid, with a median potency of 4 and a mean of 3.6. Two patients were changed from prednisolone to methylprednisolone therapy, and the ratio had a median and mean of 0.8. One patient was transferred from cortisone therapy, and the ratio was 4.2. In three instances, due to exacerbations of the underlying disease at the time of transfer to the newer steroid, no equivalent dosages could be determined.

The maximum maintenance dose was 192 mg. per day in a critically ill patient for two weeks. While she was receiving this dosage, it was noted that she had a miliary pulmonary infiltrate which subsequently proved to be tuberculous. This occurred after two and one-half months of methylprednisolone therapy. The initial chest x-ray was perfectly normal. Two months after institution of antituberculous therapy and gradual reduction of methylprednisolone dosage to a maintenance dose of 16 mg. per day, the lupus erythematosus and miliary tuberculosis markedly improved.

Adjuvant Therapy.—All patients were on a diet with normal salt intake except four who had edema due to nephropathy. They were placed on a 200-mg. sodium diet. There was evidence of sodium retention in two patients who had no nephropathy. Supplementary potassium was given to only one patient who was vomiting. Low serum potassium levels were not noted in any of the patients, even in eight who received maintenance doses of 80 mg. per day or more for as long as two and one-half months.

A routine prophylactic ulcer regimen, usually recommended for patients taking over 50 mg. per day of cortisone or its equivalent, was not used except when indicated and in one patient, noted above, who had an elevated uropepsin level. Unfortunately, peptic ulceration was not prevented in this patient. In four patients peptic ulcers had been diagnosed previously and their ulcer regimen was continued.

Gastrointestinal Studies.—Fifteen patients had upper gastrointestinal x-rays before and every few months during methylprednisolone therapy. One new ulcer, which was asymptomatic, appeared in a patient who received doses ranging from 48 to 192 mg. per day for two months prior to the appearance of a gastric ulcer at the lesser curvature. After two months of ulcer therapy and reduction of the the dose of methylprednisolone to 16 mg. per day, the ulcer was unchanged in size. An 11-year-old girl developed a shallow duodenal ulcer with melena while receiving 96 mg. of triamcinolone per day. This had healed on treatment with an ulcer regimen. Because of a lack of clinical improvement despite a marked moon-face and buffalo-hump appearance, she was transferred one month later to methylprednisolone therapy, 96 mg. per day. Anticholinergic therapy was discontinued at the time of transfer because of obstipation. Ten days later melena recurred. Repeat gastrointestinal x-rays were equivocal. The bleeding ceased with reinstitution of anticholinergic medication and reduction of the dosage of methylprednisolone. Two weeks later the patient died; at autopsy, evidence of disseminated cryptococcosis was found, as well as the changes of systemic lupus erythematosus. No evidence of gastrointestinal ulceration was noted, nor could any other bleeding point be found. In two cases the preexisting ulcers healed with continuation of methylprednisolone and ulcer therapy. These were the only patients in the series who had epigastric distress with this new steroid. In 12 cases there was no evidence of ulceration either before or during treatment. A fourth patient with a history of a healed duodenal ulcer due to steroid treatment was not given x-ray examination during methylprednisolone therapy.

Gastric analyses were performed in seven patients before and every few months during treatment with methylprednisolone. Free and total acidity values were determined before and after subcutaneous injection of 0.1 mg. per 10 kg. of body weight of histamine phosphate. Specimens were drawn every 10 minutes after injection for a total of 40 minutes. No significant changes were noted in any of the patients. Unfortunately, none of the patients who developed peptic ulcers was cooperative enough to have gastric analyses performed serially.

Twenty-four-hour uropepsin level determinations were performed by the method of West and coworkers[4] (in which the normal range is 15 to 40 units per hour) in eight patients before and during steroid treatment. One of the patients who subsequently developed an ulcer had a level of 50 units per hour prior to therapy but a normal level while receiving methylprednisolone plus an ulcer regimen. Despite this, a gastric ulcer appeared after two months of high dosage therapy, as noted above. Levels in the other seven patients remained within normal limits. Serial uropepsin studies were not available in the two other patients who had peptic ulcers.

A control group of nine patients with systemic lupus erythematous has been treated with prednisone without an ulcer regimen for periods up to 18 months. They have had serial upper gastrointestinal x-rays. One peptic ulcer has appeared.

Results of Therapy

The pattern of clinical improvement closely paralleled that obtained in systemic lupus erythematosus by previous treatment with corticotropin and other anti-inflammatory hormones. The fever abated in 24 hours, provided that the dose of corticosteroid was adequate, joint pains disappeared in several days, and pleural effusion and cutaneous lesions subsided in one to several weeks. Three patients had mild nephropathy of short duration characterized by normotension, albuminuria of about 2+, minimal edema, granular hyaline casts and red blood cells, hypoalbuminemia without hypercholesteremia, and no nitrogen retention. This completely cleared in all patients receiving methylprednisolone therapy. Seven patients had more advanced renal disease: a nephrotic picture of anasarca, elevated cholesterol levels, nitrogen retention, and urinary sediments containing fatty casts and oval fat bodies. None of these was benefited by methylprednisolone treatment. In no case was the edema aggravated by treatment with this corticosteroid, even in doses of 144 mg. per day for periods up to three weeks. Four received nitrogen mustard with amelioration of the disease process. Six of this group of seven patients were benefited by treatment with chlorothiazide (Diuril).

Table 2.—*Clinical and Laboratory Changes in Forty Patients with Systemic Lupus Erythematosus Treated with Methylprednisolone*

	Values			Cases		Triamcinolone Group
Clinical Changes	Range	Median	Mean	No.	%	(29), %
Weight, lb.						
Decreased	3-45	12	14.7	11	27.5	62
Increased	4-12	8	7	6	15.0	10
Unchanged				22	55.0	28
Inadequate data				1	2.5	
Blood pressure (mean), mm. Hg						
Unchanged				27	67.5	69
Increased	10-22	13	15	5	12.6	17
Decreased	5-20	12.5	14	8	20.0	14
Laboratory changes						
Hemoglobin, Gm %						
Unchanged				20	50.0	55
Increased	0 9-4.7	2.3	2.2	15	37.5	35
Decreased	3.0	3.0	3.0	2	5.0	10
Inadequate data				3	...	
White blood cell count, 1,000/cu. mm.^{3}						
Unchanged				14	35.0	66
Increased	1.0-8.6	3.0	3.8	20	50.0	34
Decreased	2.2-3.0	2 6	2.6	2	5.0	0
Inadequate data				4	...	
Sedimentation rate (Wintrobe, uncorrected at 60 min.)						
Unchanged				11	27.5	35
Decreased	5-46	15 5	19.0	14	35.0	31
Increased	5-12	8	8 2	4	10.0	14
Inadequate data				11		20
L. E. cells (rotary method)						
Unchanged				9	22	17
Appeared				0	0	0
Disappeared				4	10	38
Remained absent				24	60	24
Inadequate data				3	8	14
Increased in number				0	0	0

There was a decrease in weight in 11 patients (27.5%), compared to 18 (62%) of a comparable group of 29 patients treated with triamcinolone (table 2). The median loss was 12 lb. (5.4 kg.). Six patients gained weight, with a median increase of 8 lb. (3.6 kg.). Weight remained unchanged in 22 (55%) of the group, compared to 8 (28%) of the triamcinolone group. The weight changes which occurred with methylprednisolone therapy were gradual and occurred over weeks or months. Appetite stimulation was less marked with methylprednisolone than with prednisone and the older steroids. The anorexia often noted with triamcinolone therapy was not seen.

The mean blood pressure was unchanged in 27 patients (67%), compared to 20 (69%) of the triamcinolone series. It decreased in 8 patients an average of 14 mm. Hg and increased in only five patients an average of 15 mm. Hg.

Laboratory Findings.—The hemoglobin level remained unchanged in half the cases. These patients had normal levels to start with, since in most of them adequate control had been achieved with other steroids prior to transfer. The hemoglobin level increased a median of 2.3 Gm. % in 15 cases (table 2).

White blood cell counts were unchanged in 35% and in half the cases increased an average of 3,800 cells per cubic millimeter. The Wintrobe sedimentation rate (uncorrected at 60 minutes) was unchanged in 27.5% and decreased in 35% of the group; it increased in only 10%.

L. E. cell tests, performed by the rotary method, showed no change in quantity in 9 cases, full disappearance in 4, and continued absence in 24.[5] The data are comparable to those in the triamcinolone series, since in that group the majority of patients had no L. E. cells present at the time of transfer to that steroid.

Side-effects.—The side-effects are reviewed in table 3, with comparison of methylprednisolone to triamcinolone and prednisone and prednisolone in similar patient groups treated by myself. Moonfaced appearance occurred in 52% of the methylprednisolone group as against 45% of the triamcinolone series and 49% of those receiving prednisone or prednisolone. This is certainly not a significant difference. Three weeks to several months or more were required for development of this change.

Hirsutism was definitely less marked than with triamcinolone, and in the few patients in whom it occurred it was mild. Acne occurred less often—in only 10% compared to 17% with triamcinolone and 16% with prednisone or prednisolone. Marked striae formation was noted in only one patient (3%) on methylprednisolone therapy, compared to 14% of the triamcinolone series and 3% of those receiving prednisone or prednisolone.

The one side-effect which was more pronounced with methylprednisolone than with the other steroids in systemic lupus erythematosus was a tendency toward the development of ecchymoses, noted in 27% of this group as against 14% of the triamcinolone group and only 3% of those on prednisone or prednisolone therapy. Accumulation of edema was noted in only two patients, one of whom had anemia uncorrected by methylprednisolone. Diabetes mellitus did not appear in any case. Fasting blood sugar levels were repeatedly obtained in these patients, and they remained within normal limits. None of the patients had diabetes prior to treatment.

Epigastric distress after intake of the medicament was not noted. A new peptic ulcer appeared in one patient, whose case was described above. This incidence compares favorably to that with triamcinolone when used without a prophylactic ulcer regimen and to those with prednisone and prednisolone when used with an ulcer regimen (see addendum).

Muscle weakness of the type described as occurring with triamcinolone therapy was not noted in any patient.[2] One patient who initially had some transitory weakness on methylprednisolone therapy had no recurrence of it on reinstitution of therapy with this corticosteroid. The follow-up period on this patient has been nine months. This patient and one additional one in this series had had muscle weakness on triamcinolone therapy.

Comment

Methylprednisolone is an effective new unsaturated corticosteroid with minimal ulcerogenic potency. Its common side-effects are similar to those produced by the older steroids, except for the higher incidence of ecchymoses—27% as against 14% with triamcinolone and 3% with prednisone and prednisolone. Muscle weakness was not noted in any case.

Of 18 patients who had received prior steroid therapy, 2 were benefited more by methylprednisolone than by the older steroids. One was an 18-year-old girl who had progressive extensive striae formation and marked moon face, buffalo hump, and central obesity after four months of triamcinolone therapy despite reduction of dosage during the last six weeks to 6 mg. per day. Six weeks after transfer to therapy with methylprednisolone, 16 mg. per day, the striae began to fade and the patient had less activity of her illness and her appearance became more normal. A 43-year-old woman had better over-all control of her illness with methylprednisolone than with triamcinolone, prednisone, or hydrocortisone.

The advantages of this new steroid from this standpoint were not as marked as in the triamcinolone series, where 7 of 14 patients who had been treated with other steroids were given better control with triamcinolone than with other agents. This individual variability in response to the corticosteroids suggests that, if the illness is inadequately controlled by increasing doses of one steroid, occasionally transfer to another may help. As far as transferring to another hormone to eliminate undesirable side-effects is concerned, the only ones I have seen disappear (provided the effective hormonal dose is similar) are the muscle weakness and excessive striae formation induced by triamcinolone. The usual moon-face appearance is not benefited by hormone transfer. The only effective means of combating this side-effect is reduction of the dose of steroid with synergistic therapy including salicylates and antimalarials.

The incidence of new peptic ulceration in my series of patients on methylprednisolone therapy (3% of 40 cases) is the same as that noted with triamcinolone (4% of 29) and prednisone and prednisolone when used routinely in conjunction with an ulcer diet (3% of 37) (see addendum). In the methylprednisolone and triamcinolone series no routine prophylactic ulcer regimens were utilized. The occurrence of peptic ulcer in patients with rheumatoid arthritis treated with prednisone or prednisolone without a prophylactic ulcer regimen has been reported to be as high as 31%.[6]

TABLE 3.—*Side-effects of Methylprednisolone Compared to Those of Triamcinolone and Prednisone and Prednisolone*

	Methylprednisolone (40 Cases)		Triamcinolone (29 Cases), %	Prednisone and Prednisolone (37 Cases), %
	No.	%		
Moon face, buffalo hump				
After transfer from older steroids				
Increased	2	5	14.0	12.0
Decreased	1	3	0	5.0
Unchanged	9	22	14.0	17.0
Initial appearance, methylprednisolone as first steroid	6	15	14.0	15.0
Initial appearance, transfer to methylprednisolone from other steroids	3	8	3.0	0
None at any time	19	48	55.0	51.0
Total	21	52.0	45.0	49.0
Marked hirsutism	3	8	21.0	3.0
Acne	4	10	17.0	16.0
Striae (marked)	1	3	14.0	3.0
Ecchymoses (marked)	11	27	14.0	3.0
Edema	2	5	3.0	6.0
Diabetes mellitus	0	0	3.0	6.0
Epigastric distress	0	0	6.0	3.0
Peptic ulcer*	1	3	4.0	3.0
Muscle weakness	0	0	19.0	0.0

* Patients on triamcinolone therapy were not on prophylactic ulcer regimen, whereas all those on prednisone or prednisolone therapy were whenever maintenance dose was over 10 mg. per day of either drug (see addendum).

The mechanism of ulcer formation in steroid-treated patients remains unsolved. In my experience and in that of others there is no elevation of gastric hydrochloric acid or uropepsin levels. Janowitz and co-workers[7] have shown delayed healing of experimentally produced gastric ulcers. The theory of a reduction of viscosity of gastric mucus by steroids has not been confirmed.[6] The fundamental defect producing ulceration is probably inhibition of wound healing caused by a very high local steroid level in the stomach interfering with closure of normal, spontaneously induced gastric ulceration and in addition to the systemic effects of the steroids acting in a similar manner. The incidence of peptic ulcer is highest in the arthritic groups because of the associated ingestion of large amounts of salicylates and, in some cases, phenylbutazone (Butazolidin).

Summary

Forty patients with systemic lupus erythematosus have been treated with a new synthetic, unsaturated corticosteroid, methylprednisolone (Medrol), for as long as 15 months. This hormone is 1.1 times as powerful as prednisone and four times more potent than hydrocortisone as an anti-inflammatory agent. It is only 0.9 as strong as triamcinolone in this regard. The initial dosage varied from 8 mg. per day added to the therapeutic regimen of a patient with mild disease partially controlled by rest, salicylates, and antimalarials to 96 mg. per day in a critically ill patient. The average dose was 30 mg. per day, with maintenance dose of 26 mg. There was no evidence of sodium retention or potassium loss. Routine sodium restriction, potassium supplementation, and prophylactic ulcer regimens were not used.

Fifteen patients had upper gastrointestinal series prior to and every two to three months during therapy. There was evidence of new peptic ulceration in only one, treated with 48 to 192 mg. per day for two months before the appearance of an asymptomatic gastric ulcer. She had been on a prophylactic ulcer regimen because of a high control uropepsin level. In two of these serial studies, preexisting peptic ulcers were noted; these patients were the only ones who had gastrointestinal distress while taking methylprednisolone. In the 12 other cases there was no evidence of ulceration. Seven patients had serial gastric analyses performed before and during methylprednisolone therapy. No changes were noted. Eight patients had 24-hour uropepsin studies done at similar intervals. One had an elevated level prior to treatment, and she developed gastric ulcer despite a prophylactic ulcer regimen. Her uropepsin level decreased shortly after treatment was begun and before the ulcer was noted.

The pattern of clinical improvement closely paralleled that obtained by previous treatment with older steroids. There was a disappearance of all the clinical and laboratory abnormalities produced by the disease, with the exception of long-standing renal involvement.

The incidence of side-effects, such as moon face, hirsutism, acne, and striae, was about the same as was found in a similar series of patients treated with triamcinolone and with prednisone and prednisolone. However, ecchymoses occurred in 27% and were more prominent with methylprednisolone than with the older anti-inflammatory hormones, including triamcinolone. Diabetes mellitus did not appear in any patient. Muscle weakness was not noted with use of this steroid. Moon face, buffalo hump, and central obesity produced by therapy with other steroids did not disappear after transfer to an equivalent dose of methylprednisolone in any case.

Of 18 patients who had received prior steroid therapy with other anti-inflammatory hormones, only two had better control and felt better on methylprednisolone therapy than they had on that with the other corticosteroids. Methylprednisolone is a relatively safe and potent anti-inflammatory agent for initial and maintenance steroid therapy in patients with systemic lupus erythematosus.

Addendum

An additional patient with systemic lupus erythematosus for whom data are not included in this paper received 32 mg. of methylprednisolone per day for seven months without a prophylactic ulcer regimen. Her base-line upper gastrointestinal series was normal. An asymptomatic gastric antral ulcer was noted on the repeat examination at the end of this therapy. This brings the total ulcer incidence with this steroid to 2 cases out of 40, or 5%.

A review by Dr. James G. Bulgrin of the radiology department of all the gastrointestinal x-rays done on 70 patients with systemic lupus erythematosus has revealed the presence of two additional ulcers in the triamcinolone series, making a total of 3 cases out of 29, or 10%. One patient in the control group of nine persons receiving prednisone alone without an ulcer regimen has developed an ulcer, making the incidence 11% in that series.

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CLINICAL NOTES

FAULTY FUNCTION OF TABLE MODEL ETHYLENE OXIDE STERILIZER

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Ethylene oxide has been used in industry for two decades for the sterilization of materials which cannot withstand steam sterilization. Hospital applications have awaited development of equipment suitable for the gamut from small instrument sterilization in a physician's office to the sterilization of hospital equipment and bedding. A large walk-in type of ethylene oxide sterilizer has been developed [1] and is currently being used at the Peter Bent Brigham Hospital for sterilization of furniture, bedding, rugs, draperies, and equipment which cannot be steam sterilized. The process involves five steps: heating the load to 140 F; evacuation of air from the load; humidification to achieve a moisture content of 25 to 30%; introduction of ethylene oxide, inerted by the addition of carbon dioxide, to a level of 760 mg. per liter; and exposure of three hours. The whole process is automatic, and tests with spores of Bacillus subtilis and Clostridium sporogenes have shown that under the conditions of the automatic cycle sterility invariably results.

Results of Test of Sterilizer

A table model ethylene oxide sterilizer has recently been marketed under the name Ben Venue sterilizer, designed for sterilization of instruments and materials that are destroyed by exposure to steam. This sterilizer is a compact, chromium-plated cylinder with a capacity of approximately 1 liter. The capacity can be increased by the use of a 5-in. extension sleeve. The ethylene oxide used with the sterilizer is provided in steel cylinders called Steribulbs, containing a total of 12 Gm. of ingredients of which the manufacturer states that 20% is ethylene oxide and 80% is inert. A plunger device attached to the side of the cylinder impinges the Steribulb on a penetrating needle that releases the gas into the sterilizing chamber. The directions with the instrument recommend a two-hour exposure, after which the contents are assumed to be sterile. The whole process is carried out at room temperature and at the prevailing relative humidity.

Experience in testing this sterilizer has indicated that sterility does not invariably result when the accompanying directions are followed. The test organism, B. subtilis (a strain secured from Dr. L. F. Ortenzio), was grown in soil extract broth. Loops made from size 3 silk suture were dipped into a 72-hour culture and dried for at least 24 hours at room temperature according to the method suggested by Ortenzio and co-workers.[2] The contaminated suture loops were placed into paper envelopes and exposed to ethylene oxide in the Ben Venue sterilizer. After exposure, the loops were dropped into nutrient broth and incubated at 36 C for two weeks. The results are shown in table 1.

Another series of tests was conducted with use of sterility control pledgets impregnated with spores of Cl. sporogenes, prepared by the Baltimore Biological Laboratory. After exposure to the ethylene oxide these pledgets were dropped into thioglycollate broth for sterility observation over a period of seven days. The results are shown in table 2.

TABLE 1.—*Results of Test of Ben Venue Sterilizer with Bacillus subtilis–Contaminated Suture Loops*[*]

Date	Time of Exposure, Hr.	Loops Exposed, No.	Positive Results[†]	
			No.	%
11/ 1/57	2	10	10	100
11/ 1/57	2[‡]	10	10	100
11/ 1/57	2½	10	10	100
11/ 4/57	4	10	10	100
11/27/57	2	10	10	100
11/27/57	2[§]	10	10	100
12/ 2/57	7	10	0	0
12/10/57	2	5	5	100
12/11/57	3	5	5	100
12/10/57	4	5	5	100
12/13/57	5	5	5	100
12/ 9/57	6	5	4	80
12/12/57	7	5	1	20

[*] Room temperature 70-75 F, relative humidity 25-53%.
[†] Indicates growth.
[‡] Cultured one hour after removal from sterilizer.
[§] 2 ml. of distilled water placed in sterilizer.

The criticism can justifiably be made that this sterilizer was primarily designed for instrument sterilization and, since the tests noted in tables 1 and 2 involve the use of spores on silk or cotton fibers, the results are not good approximations of spores on metal instruments. To test the sterilization of contaminated steel surfaces, six stainless steel slides, measuring approximately 1 by 3 in., were contaminated with 1×10^6 B. subtilis spores. The slides were allowed to dry for 48 to 72 hours and were then exposed to ethylene oxide in the Ben Venue sterilizer. The results are shown in table 3.

Comment

The results of our tests indicate that the use of the Ben Venue sterilizer, according to the directions given by the manufacturer, is not a satisfac-

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tory method of sterilizing either spore-contaminated fiber or steel. We have not used vegetative bacterial cells in our testing, and it may very well be that this method is adequate for their destruction. However, since the word "sterilization" implies the death of all living organisms, this piece of equipment cannot legitimately be called a sterilizer.

We appreciate the fact that the dry spores used in the tests described here are extremely resistant to sterilization and have been a severe test of the sterilizing efficiency of the equipment. However, in practical application, one has no guarantee of the degree of resistance of organisms on material to be sterilized. Instruments which have become contaminated and have been allowed to dry for a day or more before sterilization can certainly be assumed to contain dessicated spores.

TABLE 2.—*Results of Test of Ben Venue Sterilizer with Clostridium sporogenes in Cotton Pledgets**

Date	Time of Exposure, Hr.	Pledgets Exposed, No.	Positive Results†	
			No.	%
10/15/57	2¼	9	6	67
10/31/57	1½	10	8	80
10/31/57	2	10	6	60
10/31/57	2½	10	8	80

* Room temperature 75 F, relative humidity 51%.
† Indicates growth.

Ethylene oxide, in both liquid and gaseous form, has been found to be an efficient sterilizing agent. However, many factors influence the death rate of organisms exposed to it—such factors as relative humidity, temperature, concentration, and degree of contamination of material to be sterilized.

It is entirely conceivable that a workable table model ethylene oxide sterilizer can be devised which will be satisfactory once these factors are taken into consideration. A heating unit incorporated in the apparatus would rapidly accelerate the rate of kill. Phillips[3] has calculated a Q_{10} of 2.74 for ethylene oxide; thus, a 10-C rise in temperature would more than double the rate of kill. Some arrangement for securing an optimum relative humidity of 28%[4] in the sterilizer would also be advisable.

TABLE 3.—*Results of Test of Ben Venue Sterilizer with Bacillus subtilis–Contaminated Stainless Steel Strips**

Date	Time of Exposure, Hr.	Strips Exposed, No.	Strips Showing Growth, No.
12/30/57	2	2	2
12/30/57	4	2	1
12/31/57	2	2	2

* Room temperature 71 F, relative humidity 27-29%.

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EXPOSURE TO BERYLLIUM.—The physician is hindered in diagnosing chronic beryllium disease by the fact that the worker-patient frequently does not know the nature of the materials with which he or those around him have worked. Furthermore, this work exposure may have terminated more than a decade prior to the onset of current clinical symptoms. . . . Although there have been no reports of beryllium disease in miners of the ore, beryl, which contains from 2% to 12% beryllium, the subsequent extraction process has been frequently implicated in the disease. The manufacture of fluorescent tubes constituted a second major source of toxic exposure in that phosphors used from 1938 to 1949 often contained from 2% to 14% beryllium, generally as zinc-manganese-beryllium silicate. This hazardous use of beryllium was discontinued in 1949 by mutual agreement of the manufacturers. No such self-regulation has applied to the "neon" sign producers, many of whom operate small backyard or garage "factories" and who may freely obtain and process beryllium oxide in the preparation of phosphors. . . . Beryllium is used in windows of x-ray tubes because it is easily penetrated by the rays and is stable at high temperatures. It is also employed in nuclear energy projects, since it readily yields neutrons under alpha particle bombardment. . . . Because of its lightness, rigidity, and resistance to heat, beryllium is today finding use in structural parts of high-velocity space vehicles. The oxide may be used in heat-resistant ceramic nose-cones. . . . Typists, clerks, engineers, and janitors, though they do not directly use beryllium, may be affected because of atmospheric contamination. Furthermore, neighborhood atmospheric contamination or beryllium-containing dusts brought home on work clothes may lead to disease in persons remote from any plant.—H. L. Hardy, M.D., and L. B. Tepper, M.D., Beryllium Disease: A Review of Current Knowledge, *Journal of Occupational Medicine,* April, 1959.

ORTHOSTATIC APHASIA AFTER CARDIAC SURGERY

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Orthostatic aphasia is a term applied to that condition in which the patient becomes aphasic when in the sitting or upright position. The cause of this phenomenon is unknown. However, it must be assumed that there exists a relative ischemia affecting the essential centers and/or the associated fiber tracts which control the motor function of speech. When a patient is in the supine position there is adequate blood supply to these areas, permitting them to function normally. Resumption of the upright position slightly diminishes this blood supply, resulting in the production of cerebral ischemia and aphasia.

After cardiac surgery numerous complications may occur. Arterial embolization during the correction of mitral stenosis is not uncommon. Bolton and Bailey[1] have reported various neurological and neuropsychiatric phenomena in the cardiac patient after surgery. However, in a series of well over 2,000 such patients operated on for valvular lesions, Bolton and Musser[2] have not observed orthostatic aphasia. To our knowledge, this case represents a complication which has not been previously reported.

Report of a Case

A 47-year-old married female was admitted to West Jersey Hospital on Jan. 28, 1959, with a history suggestive of rheumatic activity occurring in childhood; her condition had been diagnosed as acquired mitral valvular stenosis after discovery of a heart murmur 27 years prior to this admission. Though never in frank congestive failure, she had demonstrated atrial fibrillation for many years and her condition had been maintained with digitalis for a period of no less than 20 years. Her general cardiac status had progressively declined in spite of constant and diligent medical therapy, and at the time of admission her functional capacity was 2-3 according to the American Heart Association classification.

She remained symptom free until four years prior to admission, when she experienced an episode of cerebral embolization which was manifested by hemiplegia on the left. For a period of approximately three weeks the patient was aware of sensory aberrations, predominantly numbness, involving the entire left side. At this time her course proceeded uneventfully, with no evidence of residua. During the ensuing four years she had noted slowly progressing exertional dyspnea.

On Jan. 28, 1959, the patient experienced excruciating pain localized to the left popliteal space, with associated absence of the popliteal pulse and discoloration of the extremity distal to the knee. Oscillometric readings and marked local temperature decrease substantiated the diagnosis of arterial occlusion involving the popliteal vessel. A regimen of anticoagulants and supportive therapy, including lumbar block, proved effectual, and 23 days later the patient successfully withstood a mitral commissurotomy. The operation was accomplished without event, and a most satisfactory technical result was obtained.

Approximately 72 hours postoperatively, with the patient in the semi-Fowler position to facilitate expectoration, she attempted to speak and found she was unable to articulate. The bed was promptly lowered so that she was in the supine position, and within several seconds her enunciation was normal. Vital signs were immediately obtained and revealed no change from previous recordings. The patient was alert and cognizant of her condition. She demonstrated no particular concern or emotional disturbance with this experience and expressed her reaction by stating that she "felt silly" because she could not talk. Within a period of several hours it was noted that the left angle of the mouth was slightly depressed. After the initial episode she was placed in a sitting position only in the presence of a physician. A stellate ganglion block effectively produced the expected Horner's syndrome and contributed to her general supportive therapy. It is interesting to note that on each occasion her orthostatic aphasia essentially mimicked the original pattern, with no change in vital signs, clinical picture, or laboratory studies. This condition existed for a period of four days and then spontaneously subsided.

Her remaining postoperative course was punctuated by a profuse menses aggravated by anticoagulant therapy. The patient was discharged on the 11th postoperative day in good condition.

Comment

It is our belief that this patient suffered a minimal postoperative cerebral embolus which produced a relative ischemia affecting her speech

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center (Broca's area) or associated fiber tracts and that while the blood supply was sufficient to maintain this area with the patient in the supine position, thus allowing her to articulate, it was inadequate to do so in the upright position.

249 N. Broad St. (7) (Dr. Bolton).

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NATURE OF ADVERSE REACTIONS TO RADIOPAQUE AGENTS

PRELIMINARY REPORT

Sidney S. Sobin, M.D., Ph.D., Wallace G. Frasher, M.D., George Jacobson, M.D.
and
Frank A. VanEeckhoven, Los Angeles

The nature of the adverse reactions to the intravascular administration of radiopaque agents is not known.[1] Such reactions or complications vary from mild, with nausea and vomiting and urticaria, to severe, with syncope, shock, convulsions, respiratory distress, and focal hemorrhage, to fatal. They occur with intravenous urography, angiocardiography, regional aortography, and arteriography. It is difficult to arrive at an over-all estimation of reaction rates, due to different criteria of what constitutes a "reaction" as well as variables in observing and reporting. From our observations, as well as those in the literature, it would appear that reactions increase with increasing dose, concentration, and speed of injection of these substances. Although the reaction rate, in the main, has decreased with the introduction of newer agents, their increased use in a wide variety of diagnostic situations has resulted in an increased incidence of reactions.

For reasons to be detailed elsewhere,[2] we have studied the effect of the compounds diatrizoate (Hypaque) sodium and sodium diprotrizoate (Miokon sodium) on the small blood vessels at the corneal-scleral junction in man and rabbits. A modification [3] of the standard binocular dissection microscope method has provided greater facility in use of this equipment and increased light for photomicrography. The magnifications used allowed arterioles and venules of 75 μ or larger to be easily observed.

The corneal-scleral blood vessels were studied in 24 adult male patients who received roentgenographic contrast mediums for intravenous urography. None of these patients was acutely ill at the time of study. Diatrizoate sodium (30 cc. of 50% solution) or sodium diprotrizoate (20 cc. of 50% solution) was given intravenously in 45 to 60 seconds. In a few patients nausea without vomiting occurred.

In 20 of 24 persons so studied, characteristic changes occurred in the corneal-scleral vessels after the administration of these materials. These changes varied only in degree from patient to patient. The vascular alterations were first seen one to two minutes after the end of the injection. There was marked slowing of the microcirculation, and the fine granular appearance of the erythrocyte column was quickly replaced by a much coarser granularity with red blood cell masses and clear irregular intravascular plasma zones between the red blood cell masses. Variable degrees of vasoconstriction were noted in both minute arterial and venous vessels with marked irregularity in blood vessel margins resulting in a scalloped edge. At times there was almost complete pinching off of the red blood cell column and formation of sausage-like masses which moved slowly down the vascular trunk. Despite the numerous red blood cell aggregates, actual stasis did not occur. Pinched off masses moved slowly and erratically to the confluence with larger vessels and then disappeared into the more rapidly moving larger stream. There was an over-all decreased vascularity in the microscopic field. The intensity of these vascular alterations was maximal at four to six minutes after the injection, and although no attempt was made to follow the return of the vascular bed to normal in all persons, in most instances

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it had returned to its previous state 20 minutes after the administration of the radiopaque material.

Similar observations were made at the corneal-scleral vessels of immature (250-Gm.) albino rabbits lightly anesthetized with urethan. The radiopaque substances, diatrizoate sodium, sodium diprotrizoate, and sodium acetrizoate (Urokon sodium), were given through a fine catheter inserted into the jugular vein in amounts proportionate to that used in angiocardiography in man. The changes in the corneal-scleral vessels were identical to those seen in man, although the time of onset of these alterations was markedly shortened and the total reaction more intense.

These observations may provide some rational basis for the understanding of the reactions to the radiopaque agents. The precise cause and nature of the blood vessel changes and the red blood cell aggregates is not known, and only with such knowledge can the exact cause of these reactions be determined and ultimately prevented.

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This study was supported by the Los Angeles County Heart Association and Mallinckrodt Chemical Works, St. Louis.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following sixth and final paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on The Use and Abuse of Adrenal Steroids. The first five papers appeared in THE JOURNAL *on June 20 and 27 and July 4, 11, and 18, 1959, pp. 952, 1063, 1179, 1311, and 1411. The panel discussion which concluded the program is available in mimeographed form in the Secretary's Office, Council on Drugs.*

H. D. KAUTZ, M.D., *Secretary.*

STEROID THERAPY IN OPHTHALMIC LESIONS

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Since the advent of cortisone approximately a decade ago, numerous steroids and steroid derivatives have been evaluated for their ocular effects when administered locally and systemically. These include cortisone (Cortisone, Cortogen, Cortone) acetate and free alcohol, hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) acetate and free alcohol, hydrocortisone tertiary-butylacetate, prednisolone (Delta Cortef, Hydeltra, Meticortelone, Meti-Derm, Paracortol) free alcohol and acetate, prednisolone butylacetate (Hydeltra-T. B. A.), methylprednisolone (Medrol), triamcinolone (Aristocort, Kenacort), and dexamethasone (Decadron, Deronil). Not all of these have had completely adequate trial in ophthalmology. However, when topically applied, only minor differences in clinical activity have been noted. If employed in individual dosages and proper vehicles and method of administration, all have equivalent anti-inflammatory potency for ocular diseases. For ophthalmic therapy, these agents may be applied locally in solution or ointment vehicles or injected subconjunctivally. There appears to be no significant advantage to intracameral injection. They may also be used systemically. Corticotropin (ACTH, Acthar, Corticotropin, Cortrophin) is employed intravenously or intramuscularly for ocular diseases.

The present trend is to use corticosteroids in preference to corticotropin because of the ease of administration and the effectiveness of locally applied forms. Local routes are preferred over systemic ones because of the ease of administration, lower cost, and freedom from systemic side-effects, which allows treatment to be continued safely over a long period of time.[1]

It has been established that steroids do not act on the cause of ocular disease but do reduce the reaction of the tissues to an exciting agent. They

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suppress hypersensitivity reactions and inflammations due to infection, inhibit neovascularization, reduce fibroblastic activity, and interfere with some immunological reactions.[2] Minor differences in local activity have been demonstrated clinically and experimentally; e. g., hydrocortisone locally instilled has been shown to be more effective than cortisone for vernal conjunctivitis.[3] The effectiveness of each is approximately the same for other anterior segment inflammations when applied topically.

Penetration studies have revealed a difference, in ability to penetrate, of the acetate and free alcohol varieties of cortisone, hydrocortisone, prednisone (Deltasone, Deltra, Meticorten, Paracort), and prednisolone. It has also been demonstrated that the acetate variety of hydrocortisone penetrates more readily through the cornea than the more soluble phosphate and succinate forms.[4] This may account for the slightly greater anti-inflammatory action of the less soluble derivatives when administered locally.[5] Studies of penetration of systemically applied steroids did not show a clear-cut relationship between the ease of penetration and antiphlogistic action.[6]

Experimental and clinical studies over the past 10 years have revealed that, in anterior ocular inflammations, locally applied steroids are equal in effectiveness to systemically administered steroids or corticotropin.[7] In posterior segment inflammations, local routes appear to be inferior to systemically administered steroids or corticotropin. Steroids given systemically seem to be equivalent to corticotropin for most of the responsive posterior segment conditions.[8]

Since steroids are easily administered systemically, they are usually preferred over corticotropin for equally responsive conditions. However, corticotropin may be preferred for severe inflammations that threaten the functional integrity of the eye. In severe intraocular infections, corticotropin given intravenously, which mobilizes many adrenal steroids, is preferred to oral therapy with steroids for the purpose of reducing inflammatory reactions until the infecting agents can be overcome by the specific antibiotic.[9] As in other areas of the body, hormonal therapy is used in ophthalmology for the sole purpose of controlling inflammation until the ocular defenses can handle the problem; they have no curative effect on ocular diseases and possess no bactericidal or tissue-stimulating activity. In ocular pathology the effect of the hormones is not to make up a deficiency of hormones; they inhibit inflammation, whether it be due to allergic, toxic, infectious, or traumatic etiology. If the stimulus is great, the steroids may not prove adequate to block the reaction.

Topically and systemically administered steroids produce favorable results in such external inflammations as contact dermatitis, rosacea keratoconjunctivitis, vernal conjunctivitis, allergic conjunctivitis, allergic keratoconjunctivitis, marginal corneal ulcers, and phlyctenulosis. There are a number of ocular conditions that are not benefited including pemphigus and, in many cases, nodular episcleritis. Episcleritis, scleritis, and ocular manifestations of collagen disease have shown irregular responses.[10]

Steroids prove most useful in nongranulomatous uveitis of both the anterior and the posterior varieties. Uveitis due to sarcoid may respond incompletely. Recurrences are frequent and are not always quieted by additional or continued administration of steroids.

Sympathetic ophthalmia is best treated initially by intravenous administration of corticotropin and carried to the point of quiescence by steroids given systemically and locally. The continuous gradual reduction of steroids may demand a year or more until therapy is no longer required.

Occasionally, but rarely, one steroid might succeed in controlling an ocular disease in which another in large dosage has failed. Isolated examples of dramatic improvement have been seen, but this is not the usual experience of the majority of ophthalmologists dealing with degenerative diseases. Most of the results with degenerative ocular diseases are not impressive. Optic neuritis and retrobulbar neuritis seem to quiet more rapidly with the institution of steroids, particularly corticotropin given intravenously.

Steroids have been shown to be contraindicated in corneal ulcers due to herpes simplex[11] and fungi.[12] Bacterial ulcers may respond in the presence of steroids if the anti-infectious therapy has been specific, properly administered, and in adequate dosage. The same applies to conjunctivitis of similar etiologies.

In dealing with conjunctivitis, it is fairly well recognized that ideal therapy demands specific diagnosis. It is true that one cannot always be certain of etiology. Cultures and cytological studies are helpful but expensive. Most conjunctival inflammations subside spontaneously. Steroid therapy may reduce the local reaction but may interfere with natural resistance. Therefore, it is recommended that steroids not be used as a substitute for clinical acumen. One should employ less hazardous and usually less expensive medicaments such as astringents, zinc preparations, quaternary ammonium compounds, or even saline irrigations until the cause of the disease is indicated or until cultures and smears can aid in the selection of specific medicaments. After such a course, one is less likely to enhance the development of dendritic keratitis or corneal fungous infections. Both of these types of infections have increased in severity and incidence since the advent of locally administered steroids. It has been noted repeatedly that the patient undergoing local therapy with steroids may have less discomfort and see his physician less frequently; consequently, the gradual progression of the disease may go undetected until late in its course.

Fungous infections of the cornea can readily be produced experimentally by pretreatment with steroids. This has been demonstrated by Ley and Sanders[12b] and by Montana and Sery.[12c] Perhaps a safe rule to follow for the local use of steroids in external ocular disease is this: when a doubt exists as to diagnosis or to the likelihood of a favorable response to steroids, steroids should not be used.

There is also a contraindication to systemic administration of steroids in granulomatous uveitis and intraocular infections that might be of fungal or perhaps viral origins. It has been demonstrated that steroids have a disastrous influence on experimental fungal choroiditis whether this is due to Candida albicans or to *Aspergillus*.[13] The injection of steroids during the course of such an experimental infection causes exacerbation of the inflammation in a disease which is often otherwise self-limited.

Similarly, Woods has demonstrated less favorable response in acid-fast intraocular infections with steroids alone. Uveitis due to sensitivity to tuberculoprotein can react favorably to steroid administration. The difficulty is to determine the etiology. Perhaps simultaneous administration of antituberculosis drugs in adequate concentration might prevent the unfavorable effects of steroids on tuberculous uveitis. However, when one is reasonably certain of a tuberculous etiology in uveitis but cannot determine relative rate of infection and hypersensitivity, the specific antituberculosis chemotherapy should be employed first and steroids added to this later if the results have not been favorable and if the uveitis is still considered to be of tuberculous etiology.

There is some clinical evidence that steroids are not harmful in toxoplasmic uveitis. However, the diagnosis here is not certain, and the favorable results may be due to another cause.

Sympathetic ophthalmia and sarcoids are examples of granulomatous uveitis that can respond favorably to long-term therapy. However, long-term treatment has many hazards. The over-all rule that can be applied to steroids in ophthalmology would be to use steroids when long-term therapy is necessary in those ocular conditions in which no other therapy with fewer side-effects is known to be helpful. The crucial word in this sentence is "helpful," for the steroids must be known to have been helpful in the condition before they are employed on a long-term basis. Steroids should not be used simply because the ophthalmologist knows nothing else to do.

Summary

Corticosteroids and adrenocorticotropic hormones given systemically are of considerable value in the therapy of ocular disorders. There are undesirable ocular effects from corticosteroids such as the development of and/or enhancement of herpes simplex keratitis and fungal keratitis after local corticosteroid ocular instillations, and there are the possibilities of undesirable side-effects from the long-term systemic administration of corticosteroids and corticotropin. These agents should be used only for those ocular conditions in which definite benefit has been demonstrated. They should not be used simply because the physician knows nothing else to do for the ocular disorder. Steroids are of limited value in the management of infectious diseases. They certainly should not be used in the treatment of ocular infectious disease without adequate specific antimicrobic coverage. Long-term therapy with steroids in ocular disorders should be avoided unless there are specific indications.

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gree of correlation has been obtained in tests for achlorhydria in which the azure A resin method and the conventional gastric analysis by intubation were used. It should be understood, however, that, when caffeine is used as the stimulant to gastric secretion prior to the administration of the resin, the azure A method determines what might be called a caffeine achlorhydria. True achlorhydria can be determined only if the most powerful stimulants to gastric secretion, such as betazole or histamine, are used.

The azuresin test does not furnish exact quantitative results. However, it is convenient for screening patients with minor gastric symptoms that are not considered sufficiently significant to warrant the discomfort of intubation gastric analysis or other more expensive diagnostic procedures. It should not be used in lieu of more extensive examinations whenever these are indicated. When the test indicates achlorhydria, some clinicians advocate confirmation of these results by repeating the test, using histamine or betazole as the stimulant to gastric secretion. The resin test method for achlorhydria is considered useful for the diagnosis of suspected cancer of the stomach, pernicious anemia, and gastric polyps.

Azuresin is of negligible toxicity, and, to date, no instances of drug idiosyncrasy have been reported (as was sometimes the case with the older quinine resin). The test may be carried out without regard to previous or concomitant drug therapy. However, tubeless gastric analysis may be inaccurate in the presence of pyloric obstruction, severe hepatic or renal disease, abnormalities that impair intestinal absorption, urinary bladder obstruction, or in patients who have undergone total or subtotal gastrectomy.

Dosage.—Azuresin is administered orally as a single test dose of approximately 2 Gm. in the form of granules. Patients should be instructed not to eat after midnight preceding the day of the test. On the morning of the test, the patient should empty the bladder and discard the urine. Breakfast is withheld until the test is completed. Two 250-mg. tablets of caffeine and sodium benzoate are swallowed with one glass of water. One hour later, the patient voids and saves this specimen in a jar marked "control urine." Then the 2-Gm. dose of the resin is stirred well and taken in one-fourth glass of water (without chewing the granules). If any granules remain in the glass, these are consumed with a little more water. Exactly two hours after the resin is taken, the urine should be voided and the entire amount saved in a jar marked "test urine." After the last specimen has been voided, the patient may eat breakfast. The two specimens should be delivered to the physician or to a clinical laboratory as soon as convenient. The patient may continue to pass blue or green urine for a few days.

When indicated or desired, a subcutaneous or intramuscular dose of 50 mg. of betazole hydrochloride for a person weighing 100 to 250 lb. (45.4 to 113.4 kg.) or 0.0275 mg. of histamine phosphate per kilogram of body weight may be substituted for the orally given caffeine and sodium benzoate as the stimulant to gastric secretion.

Preparations: granules 2 Gm. (with comparator, color standards, and two 250-mg. tablets of caffeine and sodium benzoate).

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation cooperated by furnishing scientific data to aid in the evaluation of azuresin.

CHEMICAL LABORATORY

The Chemical Laboratory has authorized publication of the following statement.

WALTER WOLMAN, PH.D., *Director.*

Monographs of tests and assays for new and nonofficial drugs adopted by the Chemical Laboratory of the American Medical Association represent an expression of opinion as to what might constitute adequate tests and assays to serve as a reference guide to those interested in the identity and quality of a new and nonofficial drug.

Completed monographs are published in the journal *Drug Standards* for those interested in the details of the procedures. Monographs on the following drugs have appeared in the March-April, 1959, issue of that journal, except for the monograph on chloroprocaine hydrochloride which appeared in the January-February, 1959, issue. The cooperation of the listed pharmaceutical firms that furnished samples and data is acknowledged.

Chloroprocaine hydrochloride	(Maltbie Laboratories)
Procyclidine hydrochloride	(Burroughs Wellcome & Co. [U. S. A.] Inc.)
Pyrrobutamine phosphate	(Eli Lilly & Company)

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NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Azuresin (Diagnex Blue).—Azure A Carbacrylic Resin.—A complex of azure A and a polyacrylic carboxylic acid resin. Azure A is a blue dye which is chemically defined as 3-amino-7-dimethylaminophenazathionium chloride.

Actions and Uses.—Azuresin, introduced in 1958, is employed as an indicator for the detection of gastric anacidity (achlorhydria) without intubation. After oral administration of the drug, the blue dye (azure A) in the resin is displaced by the hydrogen ions of free hydrochloric acid that may be present in the stomach. A part of the displaced azure A is absorbed and excreted in the urine within two hours after administration of the resin. A stimulant to gastric secretion is given one hour before administration of the resin. Urine voided during that hour serves as a control sample. The dye content of the urine specimen collected two hours after administration of the resin is visually estimated as an indication of the presence or absence of free hydrochloric acid in the stomach. Because visual estimation of a blue dye in the urine is much less complicated than determination of urinary quinine by photoelectric fluorophotometry, azuresin has completely replaced the older quinine carbacrylic resin for tubeless gastric analysis.

Azure A in the urine is estimated by use of the color comparator which is supplied with each test unit of the drug. Two color standards representing color intensities of 0.3 and 0.6 mg. of azure A in 300 cc. of solution (0.1 and 0.2 mg.%), respectively, are also provided. After dilution of the control urine sample and test urine sample to 300 cc. each, two 10-cc. aliquots of the control urine are placed in the comparator in front of the two standards and one 10-cc. aliquot of the test urine between the two controls. Visual comparison is then made between the color intensity of the two standards and a 10-cc. aliquot of the test urine. If the color of the test urine is darker than that of the 0.6-mg. standard, the patient is presumed to have secreted free gastric hydrochloric acid, and the test is complete at that point. Since azure A may be excreted in the urine in its blue form or a conjugated colorless form or both, the test should not be interpreted as negative (achlorhydria) until any colorless form present has been oxidized to the blue form. Thus, if the color of the test urine is lighter than that of the 0.6-mg. standard, all samples are acidified with two drops of 10% hydrochloric acid to give a pH between 2 and 4, heated for 10 minutes in a boiling water bath, and allowed to cool for two hours. If a red color results from the addition of hydrochloric acid, too much has been added and second aliquots must be used with less hydrochloric acid. It is important to allow the full two hours for cooling prior to rereading color intensities, since this period of time is required for the full color to develop. After the cooling period, visual color comparison between the test urine and the two standards is done as described previously. If the color intensity of the test urine lies between that of the 0.6-mg. and that of the 0.3-mg. standard, this is interpreted as presumptive evidence for hypochlorhydria. An intensity less than that of the 0.3-mg. standard is presumptive evidence for achlorhydria. A high degree of correlation has been obtained in tests for achlorhydria in which the azure A resin method and the conventional gastric analysis by intubation were used. It should be understood, however, that, when caffeine is used as the stimulant to gastric secretion prior to the administration of the resin, the azure A method determines what might be called a caffeine achlorhydria. True achlorhydria can be determined only if the most powerful stimulants to gastric secretion, such as betazole or histamine, are used.

The azuresin test does not furnish exact quantitative results. However, it is convenient for screening patients with minor gastric symptoms that are not considered sufficiently significant to warrant the discomfort of intubation gastric analysis or other more expensive diagnostic procedures. It *should not be used in lieu of more extensive examinations* whenever these are indicated. When the test indicates achlorhydria, some clinicians advocate confirmation of these results by repeating the test, using histamine or betazole as the stimulant to gastric secretion. The resin test method for achlorhydria is considered useful for the diagnosis of suspected cancer of the stomach, pernicious anemia, and gastric polyps.

Azuresin is of negligible toxicity, and, to date, no instances of drug idiosyncrasy have been reported (as was sometimes the case with the older quinine resin). The test may be carried out without regard to previous or concomitant drug therapy. *However, tubeless gastric analysis may be inaccurate* in the presence of pyloric obstruction, severe hepatic or renal disease, abnormalities that impair intestinal absorption, urinary bladder obstruction, or in patients who have undergone total or subtotal gastrectomy.

Dosage.—Azuresin is administered orally as a single test dose of approximately 2 Gm. in the form of granules. Patients should be instructed not to eat after midnight preceding the day of the test. On the morning of the test, the patient should empty the bladder and discard the urine. Breakfast is withheld until the test is completed. Two 250-mg. tablets of caffeine and sodium benzoate are swallowed with one glass of water. One hour later, the patient voids and saves this specimen in a jar marked "control urine." Then the 2-Gm. dose of the resin is stirred well and taken in one-fourth glass of water (without chewing the granules). If any granules remain in the glass, these are consumed with a little more water. Exactly two hours after the resin is taken, the urine should be voided and the entire amount saved in a jar marked "test urine." After the last specimen has been voided, the patient may eat breakfast. The two specimens should be delivered to the physician or to a clinical laboratory as soon as convenient. The patient may continue to pass blue or green urine for a few days.

When indicated or desired, a subcutaneous or intramuscular dose of 50 mg. of betazole hydrochloride for a person weighing 100 to 250 lb. (45.4 to 113.4 kg.) or 0.0275 mg. of histamine phosphate per kilogram of body weight may be substituted for the orally given caffeine and sodium benzoate as the stimulant to gastric secretion.

Preparations: granules 2 Gm. (with comparator, color standards, and two 250-mg. tablets of caffeine and sodium benzoate).

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation cooperated by furnishing scientific data to aid in the evaluation of azuresin.

CHEMICAL LABORATORY

The Chemical Laboratory has authorized publication of the following statement.

WALTER WOLMAN, Ph.D., *Director.*

Monographs of tests and assays for new and nonofficial drugs adopted by the Chemical Laboratory of the American Medical Association represent an expression of opinion as to what might constitute adequate tests and assays to serve as a reference guide to those interested in the identity and quality of a new and nonofficial drug.

Completed monographs are published in the journal *Drug Standards* for those interested in the details of the procedures. Monographs on the following drugs have appeared in the March-April, 1959, issue of that journal, except for the monograph on chloroprocaine hydrochloride which appeared in the January-February, 1959, issue. The cooperation of the listed pharmaceutical firms that furnished samples and data is acknowledged.

Chloroprocaine hydrochloride	(Maltbie Laboratories)
Procyclidine hydrochloride	(Burroughs Wellcome & Co. [U. S. A.] Inc.)
Pyrrobutamine phosphate	(Eli Lilly & Company)

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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CLINICAL IMPORTANCE OF POTASSIUM

RENEWED interest has been stimulated in the element potassium. Evidence is accumulating that both hyperpotassemia and hypopotassemia are clinically significant disorders. Even the cardiotoxic property of potassium has a direct clinical application in the use of potassium citrate to induce complete, temporary arrest of the heart in surgery.[1]

Much that has long been known about potassium metabolism remained clinically inapplicable in the past because of the lack of good chemical methods to determine the concentration of potassium in body fluids and tissues. The first general facts about salt balance, about the harmful effects of deficiencies and excesses of potassium, and about its curious distribution between intracellular and extracellular fluids were obtained either by indirection or by difficult analytical methods. Since that time research in this field has been expedited by advances in chemistry. Advances in physics have likewise brought improved understanding of many other medical aspects of potassium, for example, its radioactivity, which was at one time considered as a possible cause of the spontaneous activity of the heart. It is not easy, today, to picture the difficulties, the confused concepts and inadequate apparatus, under which the early work on potassium was done. The advent of radioactive isotopes has made it possible to follow the movements of potassium atoms through biological structures, with results so rich as to be almost overwhelming, and the advent of the flame photometer, with related electronic apparatus, afforded a convenient, accurate method that all but revolutionized the study of potassium deficits or surfeits in body fluids and tissues.[2]

The kidneys, when healthy, are able to rid the body quite promptly of excesses of potassium that may enter by injection or ingestion. This fact is basic in clinical applications. When a heart is to be arrested for surgical purposes, potassium citrate is injected into the proximal aorta; it is kept there, and its action is confined to the coronary system, by the clamp on the aorta. When the heart is to be restarted after the operation, the first coronary sinus blood with its high potassium content is allowed to overflow from the heart, but the kidneys are relied on to dispose of whatever potassium gets into the general circulation.[1] In this situation, with healthy kidneys, the potassium is handled easily, but in other situations, if the kidneys are diseased, even small amounts of potassium can be fatal.[3] The concentration of potassium in normal plasma is given as 5 mEq. per liter (about 20 mg. per 100 cc.). Rising concentrations cause bradycardia, heart block, and finally (at about 20 mEq. per liter or 80 mg. per 100 cc.) cardiac arrest.

Conversely, however, it is also possible to deplete the body's store of potassium, 98% of which is stated to be intracellular.[4] There is reason to believe that potassium can be lost by way of diseased kidneys. Twelve renal or extrarenal conditions that may cause a potassium-losing nephritis have been listed by Mudge.[5] The extent and seriousness of the resulting derangements could be predicted from the immense literature on salt balance, membrane permeabilities, acid-base balance, erythrocyte activity, and axone physiology. The clinical manifestations of hypopotassemia were recognized by Aitken and colleagues in 1937.[6] Developments in adrenal physiology since then have led to recognition of aldosterone as an important hormone and of aldosteronism as a possible cause of hypopotassemia. A case reported by Alsted and Halberg [7] illustrates at once the difficulty and the importance of distinguishing between primary aldosteronism and primary renal hypopotassemia. It is necessary, in any case, to keep in mind the fact that potassium can be lost from the body by way of the kidney.

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Potassium can also be lost by way of the intestine. Striking cases of hypopotassemia from this cause have been described by Roy and Ellis.[8] A 70-year-old man was found to be losing potassium as a result of a rectal adenoma. He had frequent voiding of copious watery feces. The rectal fluid had an extremely high potassium content (28 mEq. per liter). Recognition of the patient's potassium deficit explained his circulatory collapse and made it possible to prepare him adequately for surgery, so that he made an excellent recovery. The other case was that of a 56-year-old woman, who likewise had lost potassium by a watery discharge by rectum as a result of a tumor of the large intestine. Both a high potassium content of the discharge and a low concentration of potassium in her serum were established by chemical analysis. Recognition of the hypopotassemia again made it possible to treat her circulatory collapse successfully and to carry her safely through the necessary surgery.

The need of more refined diagnosis in cases of dehydration, acidosis, and salt imbalance is clearly revealed by such cases. Disturbances of potassium metabolism, as pointed out by Thorn and his colleagues in the instance of primary aldosteronism,[8] can be life-threatening. In some situations potassium medication will ameliorate symptoms; in others, it will aggravate them. Clearly such phrases as "saline solution," "isotonic salt solution," "physiological saline," and "Ringer's solution" impede progress by their inexactness and can cause real trouble in the clinic. The terms are not even qualitatively satisfactory. They do not indicate which saline compounds are to be used, whether they are to be isotonic with plasma or tears, or which of the various Ringer formulas is intended. Certainly the amount of potassium needs to be specified. Perhaps there is also a general need for short, precise ways of designating solutions to be given intravenously in adjusting a patient's water and electrolyte balance. In the meantime analytical chemists and electronic engineers might well continue their search for more accurate, quick, and less expensive methods of diagnosing the patient's requirements of sodium and potassium.

BIOCHEMISTRY AN AID TO PHYSICIANS

The rapid evolution of new diagnostic and therapeutic techniques is an obvious result of the ever-increasing rate of scientific research. Less obvious is the fact that some fundamentals of medical science are being transformed by the accumulation of biochemical knowledge, thus making understandable some previously incomprehensible biological phenomena. As long as 28 years ago, in an editorial, The Journal stated:

"Physiologic chemistry—or biochemistry, as it has been commonly designated more recently—has long since come of age. The subject has become an important and integral part of the study of medicine and the practice of the art. The special technic of biochemistry has been introduced into clinical diagnosis to such an extent that it competes in prominence with physical procedures and with bacteriologic and immunologic methods of examination and research."

In more recent years biochemistry has developed an importance which predicts that medical science in the future will be taught and applied still more widely in terms of biochemical events.

Medical science is entering a phase now in which many aspects of medicine, such as inborn errors of metabolism, intermediary metabolism, energy transfer, infection by bacteria and viruses, mental processes, gene and chromosome composition, and many others are being studied and interpreted at the molecular level. Some of the most intense study in biochemistry has been on the structure and function of enzymes and the interrelationships of the enzyme systems in the body processes. Knowledge in this field has increased to a stage where many of the balanced mechanisms of enzymatic body reactions are understood in stepwise detail.

These changes pose an important problem to practicing physicians. However difficult it may be to keep abreast of this new knowledge, it seems apparent that the practice of scientific medicine in the future will depend in large part on the realization of its impact. Despite the complexity of these newer relationships, their importance makes it desirable, at least, for physicians to attempt to gain insight into the current trends in medicine that are influenced by biochemistry.

The Journal believes that it can be of further help to physicians in calling attention to biochemical advances that are closely related to the practice of medicine. To this end there will be published at short intervals a series of editorials on this subject. The first one will appear in The Journal, August 8.

THE SECOND WORLD CONFERENCE ON MEDICAL EDUCATION

UNDER THE AUSPICES OF

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

In this, my first President's Page since taking office at the annual meeting last month in Atlantic City, I want to thank the entire profession for the many honors and courtesies shown me during my year as president-elect. I also want to pledge my utmost energy and dedication to the duties of the year ahead. My goal is to be a vigorous, articulate spokesman for the American Medical Association in these difficult, changing times.

One of our major problems today is the relationship between medicine and the various types of third parties involved in the organization, provision, and financing of medical services. Until last month we had no definitive policy on this complex subject. Now, as a result of the A. M. A. House of Delegates' action on the report of the Commission on Medical Care Plans, we do have a policy.

Contrary to some reports and interpretations, the House action in Atlantic City did not constitute a change in A. M. A. policy. Instead, it should be viewed as the first establishment of a broad policy which naturally will be subject to constant study, clarification, and revision in the years ahead.

In considering Part I of the Commission report, the House received all findings and conclusions as "information only." This means that statements in those parts of the report cannot be cited out of context as official A. M. A. policy. However, the House took definite action on the Commission's 39 recommendations, accepting 36 without change and rewording three others which involved miscellaneous and unclassified plans.

Probably the most significant action came on Recommendation B-16, which was changed to read:

"The American Medical Association believes that free choice of physician is the right of every individual and one which he should be free to exercise as he chooses. Each individual should be accorded the privilege to select and change his physician at will or to select his preferred system of medical care, and the American Medical Association vigorously supports the right of the individual to choose between these alternatives."

That, as I interpret it, reaffirms our fundamental faith in the principle of freedom of choice, but it also recognizes the patient's right to select the type of medical care plan he wants—including a closed panel plan.

The House also emphasized the "far-reaching significance" of Recommendation A-7, which says:

"'Free choice of physician' is an important factor in the provision of good medical care. In order that the principle of 'free choice of physician' be maintained and be fully implemented, the medical profession should discharge more vigorously its self-imposed responsibility for assuring the competency of physicians' services and their provision at a cost which people can afford."

In other words, if we are to give full meaning and value to the principle of freedom of choice, we must establish effective mechanisms to discipline that small minority of physicians whose actions bring discredit to the entire profession.

From the long-range point of view, some of the most important Commission recommendations are those urging increased activity by state and county medical societies and the A. M. A. in such areas as continuing study, better liaison, closer attention to legal and legislative factors, and development of guides for the relationships between medicine and the various types of third parties.

To implement A. M. A. activities, the House also approved a seven-point program for immediate attention by the Division of Socioeconomic Activities.

I urge every physician to study the Commission report and to support efforts to carry out the recommendations as adopted.

Louis M. Orr, M.D.
Orlando, Fla.

ORGANIZATION SECTION

LETTER REGARDING PUBLIC ASSISTANCE AND DISABILITY CLAIMS

Hon. Burr P. Harrison, Chairman
Subcommittee on Administration
of the Social Security Laws
Committee on Ways and Means
House of Representatives
Washington, D. C.

Dear Congressman Harrison:

This is in further reference to your letter of April 6, 1959, concerning the activities of the Subcommittee on Administration of the Social Security Laws, of which you are Chairman.

As I advised you on April 15th, the American Medical Association is very much interested in the assignment of your Subcommittee and is appreciative of the opportunity of supplying you with certain information.

The Association has for many years been interested in the Social Security Act and has worked closely with those charged with the administration of the programs established under the various sections of the statute. We have also, on numerous occasions, testified before committees of the House of Representatives and the Senate concerning proposed amendments to the Act.

Inasmuch as your Subcommittee's current primary interest is in the administrative complexities of the present law, I shall not dwell at any length on the views of the Association with respect to the numerous bills introduced in the 86th Congress which propose amendments of a medical nature to the Social Security Act. I would, however, respectfully invite your attention to the testimony presented by the Association to the House Ways and Means Committee on H.R. 9467 during the 85th Congress. A number of similar and identical bills have been introduced this year and are now pending before the House Ways and Means Committee.

The other item on this same subject to which I would invite your attention is the letter dated March 5, 1959, from Dr. Leonard Larson, the Chairman of the Board of Trustees of the American Medical Association, to the House Ways and Means Committee. I am enclosing copies of these two statements for your ready reference.

Although, as stated earlier, we have had a continuing interest in numerous provisions of the Social Security Act, our comments at this time are confined to the Public Assistance and the Old Age, Survivors and Disability Insurance programs.

As presently organized, the four Public Assistance programs are separate entities, independently financed. In the medical care programs for Public Assistance recipients, the states are more and more turning to "vendor payment" methods for at least a part of the medical, hospital and auxiliary services provided. As a result, Public Assistance recipients, under different programs in the same state, are frequently eligible for radically different levels of medical care.

The House of Delegates of the American Medical Association in December, 1958, recommended that the Social Security Act be amended "to permit states to combine the present four Public Assistance medical programs into a single medical program, administered by a single agency and making available uniformity of services to all eligible Public Assistance recipients in the state." The Association has made this recommendation because it believes that such a step would help to eliminate confusion, waste and duplication resulting from the present multiplicity of programs. The Association also believes that a uniform program would tend to promote higher quality medical care.

We would suggest, therefore, that your Subcommittee consider the advisability of studying the variation in the amount of expenditure for medical services under the several programs in the states, with a view to determining the relative effectiveness of combining these, at the state's prerogative, into a single Public Assistance medical program.

The Association, through its Committee on Indigent Care, has noted an insufficiency of statistics concerning the medical care provided under the Public Assistance program. Some states provide very general data on medical expenditures, some provide data as to the amount expended for each type of medical service; few, apparently, can provide details such as the cost per patient for each type of service, the specific illnesses or disabilities treated, the operations performed, or information as to which personnel or facilities provided the majority of these services. The value of good medical statistics which could be potentially available under the Public Assistance programs suggests that the Subcommittee might well study the possibility of encouraging more complete and uniform reporting by state agencies.

It is also noted that, at the Federal level, the medical staff of the Bureau of Public Assistance is extremely limited. In view of the growing importance of medical care under this program, as well as the confusion caused by recent legislative changes at the state level, the Subcommittee might also consider the question of whether the present staff is sufficient to provide adequate counselling to the states on changes in their individual programs. Consideration should also be given to the question of whether sufficient liaison has been maintained with the various professional organizations actually providing medical care. Since there are no physicians on the recently appointed Social Security Advisory Committee, it might be suggested that a special medical advisory committee be established.

Section 1002 (a) (10) of the Public Assistance provision of the law states, in part, that "in determining whether an individual is blind, there shall be an examination by a physician skilled in the diseases of the eye, or by an optometrist, whichever the individual may select." It is our suggestion that this section be amended by striking the words "or by an optometrist, whichever." We believe that to grant optometrists the right to make examinations for determining blindness can, in individual cases, result in a failure to ascertain the cause of blindness and thus prevent the administration of necessary medical rehabilitative care. The application of medical skills by a doctor of medicine will help insure the detection and successful treatment of the organism and systemic causes of blindness. Unfortunately for the patient, such diagnosis and treatment cannot be provided by optometrists.

The particular areas of concern to medicine in connection with the administration of this program, under Title II of the Act, are related to the evaluation of "disability" for OASDI claims and requests for information long after the doctor's examination.

In the first instance, the applicant for disability coverage is expected to pay the examining physician for the initial examination. Since many of these applicants are unable to pay, the physician frequently provides this service without charge. However, if the first examination is insufficient for the purposes of OASDI, the program may then pay a physician for consultation, or reexamination of the applicant. The Subcommittee might well study the confusion inherent in such a system, particularly since the reexamination is sometimes by the same physician who made the original examination.

In the second instance, cases are reported where the OASDI has requested medical data up to fifteen years after the physician encountered the case. Obviously, it is not reasonable to expect the physician's personal recollection or records to remain completely adequate over such a long period of time. The Subcommittee might wish to study the effects of such long-delayed requests for data on the over-all efficacy of the program.

If the American Medical Association can be of additional assistance in connection with the efforts of your Subcommittee, I hope that you will either call on me or on the staff of the Washington Office of the Association.

Sincerely yours,
F. J. L. Blasingame, M.D.
Executive Vice-president.

CONSULTANTS TO A. M. A. INSURANCE COMMITTEE

Ten persons, five of whom are physicians, have agreed to serve as consultants to the Committee on Insurance and Prepayment Plans of the Council on Medical Service. They are:

Richard J. Ackart, M.D., executive director, Virginia Medical Service Association, Virginia Hospital Service Association, Richmond, Va.
James P. Donelan, M.D., vice-president and medical director, Guarantee Mutual Life Insurance Co., Omaha
Mr. J. F. Follmann Jr., director of information and research, Health Insurance Association of America, New York City
Charles G. Hayden, M.D., executive director, Massachusetts Medical Service, Boston
H. Close Hesseltine, M.D., University of Chicago, Chicago
Mr. William Martin, Martin, Clearwater and Bell, New York City
Mr. John H. Miller, vice-president and senior actuary, Monarch Life Insurance Company, Springfield, Mass.
Mr. E. R. Paolini, vice-president–general manager, California Physicians' Service, San Francisco
Mr. James E. Stuart, executive vice-president, Blue Cross Association, New York City
Ennion S. Williams, M.D., vice-president and medical director, Life Insurance Company of Virginia, Richmond, Va.

With this added talent available on a consultant basis, the Committee and Council not only will be able to augment previous activities relating to health insurance and prepayment plans but also will be in a position to deal more effectively with other facets of insurance which involve the medical profession.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

REVISION OF ESSENTIALS OF APPROVED RESIDENCIES IN OTOLARYNGOLOGY

The following revision of the Essentials of Approved Residencies as they apply to Otolaryngology was approved by the House of Delegates at the Annual Session of the American Medical Association in June, 1959. These new Essentials replace Section II—Otolaryngology, on pages 28-29 of the Essentials of Approved Residencies, as revised to Dec. 5, 1958. **The reader's attention is directed particularly to the second paragraph under "Duration of Training."**

WALTER S. WIGGINS, M.D., *Secretary.*

II. Otolaryngology

Duration of Training.—Prior to July 1, 1960, residencies in otolaryngology which are designed to meet the requirements of the Council on Medical Education and Hospitals of the American Medical Association, the American College of Surgeons, and the American Board of Otolaryngology should include, after one year of internship, three years of progressive training in the specialty. One of these years may be spent in an approved residency in general surgery or medicine, or an additional year of rotating internship.

After July 1, 1960, residencies shall be of four years' duration, of which three must be progressive training in the specialty. The four years must include one year in an approved residency in general surgery, preferably before the special training. It is emphasized that the above are minimal requirements for certification and as a foundation for further development in the broad field of otolaryngology.

Scope of Training.—Residencies in otolaryngology should offer a broad training and should preferably include some experience in closely related fields of surgery. Adequate clinical and operative experience should be provided. Essential equipment for diagnosis and treatment should be available, including all special apparatus. The clinical material should be sufficient in variety and amount to provide adequate training in the various divisions of the specialty.

Adequate experience in bronchoesophagology, allergy, anesthesiology, maxillofacial surgery, and surgery of the neck, as they relate to otolaryngology, must be provided. The training shall include a systematic course of instruction with demonstrations on clinical and technical subjects pertinent to the various phases of otolaryngology.

As stated in the general requirements (Section 7, Part I), it is not essential, or even desirable, that all hospital residencies should adopt exactly the same program, or that they should offer a rigidly uniform sequence of experience. It is essential, however, that all hospitals participating in graduate training should be able to meet the fundamental requirements for an approved program and, either alone or in collaboration, should attain comparable results in the quality of training and in the experience obtained.

A program need not necessarily be confined to a single hospital. In programs involving two or more hospitals, it is essential that the training programs be organized by the parent hospital, with progressive responsibility for the residents. Collaborative programs can be developed where two hospitals of graduate training caliber have complementary clinical resources which can be combined to advantage in developing an acceptable program.

Application of Basic Medical Sciences.—There should be training in the applied anatomy of the ear, nose, throat, neck, chest, and esophagus, including the related nervous system. Applied microbiology, biochemistry, embryology, pathology, pharmacology, and physiology should be included and should be closely correlated with the clinical experience. Frequent departmental conferences for a detailed discussion of problem cases are important, as are also the clinicopathological conferences. The residents should study and discuss with the pathologist all tissues removed at operation, and all autopsy material from patients on their services. It is desirable to have the residents assigned for a period of service in the department of pathology.

Surgical anatomy should be stressed by the attending surgeons in discussing surgical cases with the residents, and also by the pathologist, as far as is possible, in the performing of autopsies. In addition, opportunity for the residents to work out special anatomic problems by performing regional dissections should, if possible, be provided.

Research offers an important opportunity for the application of the basic sciences in clinical problems. Reasonable facilities for research by the residents should be provided, together with stimulating guidance and supervision.

Surgical Staff.—The surgical staff should be composed of surgeons who are highly qualified in both surgical skill and judgment. It should be properly organized and harmonious, with the designated head or chief of service responsible for the quality of work done in the department. The position of chief of service should not be rotated as an honorary appointment, but should be held by the surgeon best fitted for this responsibility. The members of the staff should have a real interest in teaching and in the welfare of the residents, and must be willing to give the time and effort required by the educational program.

Clinical Material.—The hospital must be able to provide an adequate number and variety of surgical patients. Arbitrary figures cannot reveal these considerations accurately. Under ordinary circumstances, however, a general hospital, to support a residency in otolaryngology, should have annual admissions to that service numbering approximately 300 to 500 patients. The hospital must be able to provide an adequate number and variety of service cases. This is essential to give the progressive operative experience necessary for the resident. The residency program should be organized so that the residents will hold positions of increasing responsibility for the care and management of patients. The residents shall have sufficient operative experience to acquire surgical skill and judgment through the performance of surgical operations with a high degree of responsibility, but under circumstances providing adequate opportunity for consultation and advice.

An approved residency in otolaryngology should include a well-organized and well-supervised, active outpatient service.

A hospital which limits its clientele to special types of cases may, if otherwise qualified, be approved as a collaborating hospital if its residency is an integral part of an approved comprehensive program.

The provisions of the general requirements (Sections 1 to 9) must also be met for approval.

Residents who plan to seek certification by an American Board should communicate with the secretary of the appropriate board, as listed in Section V, to be certain regarding the full requirements for certification.

GOVERNMENT SERVICES

AIR FORCE

First Aid Training Kit.—The Gunter Air Force Base, Ala., branch of the School of Aviation Medicine has developed an inexpensive and simple training kit which will enable military or civilian nonmedical personnel to teach anyone the fundamentals of emergency medical care in one-third the time previously required. In announcing the development of the teaching kit, the Air Force surgeon general said that the kit had simplified the teaching of basic emergency medical care to the point where practically anyone who can read may now teach others emergency medical care in the field. The teaching kit covers the basic emergency field treatment of radiation exposure, shock, cuts, wounds, burns, and movement of injured persons. It weighs only 75 lb. and probably could be mass produced at an estimated cost of less than $100 each.

Personal.—Major Gen. Olin F. McIlnay, deputy surgeon general of the United States Air Force, will retire on July 31 after more than 30 years active military service and Brig. Gen. John K. Cullen, U. S. A. F., M. C., will become Deputy Surgeon General of the United States Air Force.—Col. Raymond T. Jenkins, U. S. A. F., M. C., will become director of plans and hospitalization in the office of the surgeon general on Aug. 1 and Col. Herbert H. Kerr, U. S. A. F., M. C., will become deputy director of plans and hospitalization. Col. George H. Kojac, U. S. A. F., M. C., will replace him as chief of the plans and operations division.—Col. Charles H. Morhouse, Fifth Air Force surgeon, was appointed to the rank of brigadier general.

ARMY

Personal.—A commendation ribbon with metal pendant was awarded to Col. Arthur J. Carbonell for service as commanding officer and surgeon of the Patterson Army Hospital at Fort Monmouth. Having completed his tour of duty at that station, Colonel Carbonell has been assigned as surgeon of the VII Corps in Germany.

NAVY

Personal.—In June Rear Adm. Edward C. Kenney, M. C., U. S. N., was made deputy and assistant chief of the bureau of medicine and surgery. He succeeded Rear Adm. Bruce E. Bradley, M. C., U. S. N., who became commanding officer of the National Naval Medical Center, Bethesda, Md.—Capt. Gerald J. Duffner, M. C., U. S. N., reported to the bureau of medicine and surgery for duty as director, submarine medicine division.

VETERANS ADMINISTRATION

Personal.—Dr. Granville A. Bennett, dean of the University of Illinois College of Medicine, was appointed to the Veterans Administration advisory committee on education as a replacement for Dr. John B. Youmans, former dean of Vanderbilt University Medical School, who resigned his committee membership on accepting appointment as technical director of research at the Army Medical Research and Development Command in Washington, D. C. This five-man committee of medical educators meets at least once yearly in Washington, D. C., to advise the VA chief medical director on matters pertaining to conduct of the VA medical education program and on medical school deans committee-VA relationships.—The Veterans Administration chief medical director's commendation, highest award given by the VA department of medicine and surgery, was presented to Dr. Edwin W. Straus of the agency's Lexington, Ky., hospital. Dr. Straus was cited for his outstanding contributions to the VA patient care and medical research programs and for his studies of chemotherapy in psychiatry.

PUBLIC HEALTH SERVICE

Personal.—The National Cancer Institute's Board of Scientific Counselors, established in November, 1957, consists of six outstanding nonfederal scientists who periodically make recommendations concerning the research conducted by the National Cancer Institute. On July 1, Dr. Phillip P. Cohen of the University of Wisconsin became chairman of the board, succeeding Dr. Wendell Stanley of the University of California, who remains on the board as a member. Dr. Jacob Furth, Children's Cancer Research Foundation, Boston; Dr. Hugh Roland Butt, Mayo Foundation, Rochester, Minn.; and Dr. J. Englebert Dunphy, University of Oregon Medical School, Portland, also became members of the board in July.

Health Statistics.—Not counting military personnel or civilians in mental or other long-term institutions, the American people had, all told, about 24 million impairments in the period July, 1957, through June, 1958. These impairments included such chronic or permanent defects as paralysis, deformity, and total or partial loss of hearing and vision. The rate of impairment was 141.4 per 1,000 persons in the civilian, noninstitutional population. The report does not show the total number of persons with impairments, since many people, particularly older people, have more than one impairment. Blindness, defined as the inability to read ordinary newsprint even with the help of glasses, was reported for an estimated 960,000 people, a rate of 5.7 per 1,000 persons. In addition, 2,064,000 people were reported to have visual impairments less severe than blindness, the rate being 12.3 per 1,000. About 109,000 persons were reported as totally deaf, a rate of 0.6 per 1,000 persons; and other hearing impairments affected 5,714,000 persons, a rate of 33.9 per 1,000. Of all impairments, 33% were caused by injury. The impairments with the highest percentage rate due to injury were loss or defects of extremities. The types least often due to injury were speech defects and blindness. Impairments increased with advancing age from 52.9 per 1,000 persons at ages under 25, to 615.0 per 1,000 at ages 75 and over. Of all impairments reported, 82.2% of the patients had been attended by a physician at some time. The new report is entitled "Impairments, by Type, Sex, and Age, United States, July 1957—June 1958," Public Health Service publication no. 584-B9. Copies are for sale by the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 25 cents a copy.

FOOD AND DRUG ADMINISTRATION

Chewing Gum Won't Slim You.—The Food and Drug Administration seized 90,000 chewing gum tablets offered as a "no-diet" reducing treatment at $1 for a 20-tablet bottle. The product was alleged to be misbranded in that false representations were contained in the labeling and in sales promotion materials. These included a display carton and card, box label and insert, and a newspaper mat and tear sheet entitled "Eat What You Want—Yet Lose Up to 3-5-9 Pounds A Week," and a tear sheet entitled "Eat What You Want—Yet Lose Pounds and Inches Fast."

Seaweed Debunked.—Since eating seaweed will not assure good health, the Food and Drug Administration seized 65,000 5-grain tablets of "Pure Pacific Sea Kelp" promoted with cure-all claims at $4.50 per bottle of 1,000 tablets. The Kingsport, Tenn., dealer bought the tablets in bulk; repackaged and relabeled them in his name, and prepared promotional leaflets entitled "Are You Starving?" and "Food and Your Body." The FDA alleged that it was misbranding in that the tablets were falsely claimed to furnish adequate amounts and proportions of all the minerals, trace elements, and basic materials necessary to life, and for proper nourishment and good health. Seaweed is a source of iodine, already supplied adequately in the diet in iodized salt, and a single 5-grain kelp tablet unnecessarily supplies 58 times the minimum daily requirement for iodine. There is no general need for supplementing the diet with manganese, copper, alginic acid, chlorophyll, mannitol, or zinc—all offered as essential nutrients on the product label. The dealer claimed the tablets would produce will power, vigor, and stamina; coagulate blood in wounds; prevent tuberculosis, rickets, and excessive weight; distribute hormones in the body; stimulate memory; harden bones and teeth; build brain and nerves; maintain normal heartbeat; and prevent hardening of the arteries and cataracts.

MEDICAL NEWS

ARKANSAS

Dr. Rhine Honored.—Hundreds of friends honored Dr. Thomas E. Rhine recently at the anniversary celebration of the 60th year of his practice in Thornton. Dr. Rhine, 83, who spent the first year of his practice at Locust Bayou before coming to Thornton, has reportedly delivered 10 children and 57 grandchildren of a woman whom he had also delivered.

CALIFORNIA

Grants for Cardiovascular Studies.—The Los Angeles County Heart Association announced the award of $199,783.75 to investigators working at local medical research centers for the study of cardiovascular diseases, effective July 1. Dr. Mitchel D. Covel, Research Committee chairman, said the awards are for work to be performed during the next 12 months. Included in the grants are funds for support of the association's Cardiovascular Research Laboratory at UCLA, two established investigators, four research fellows, and 16 grants-in-aid. An additional $15,000 in awards will be made by the Long Beach Heart Association to investigators working at hospitals there.

COLORADO

New Faculty Members.—The appointment of three new full-time members of the faculty was announced by Dr. Robert J. Glaser, dean of the University of Colorado School of Medicine, Denver. The three are all graduates of Harvard Medical School, Boston. Named professor and head of the department of radiology is Dr. David M. Gould, who currently occupies a similar position at the University of Arkansas Medical Center, Little Rock. He succeeds the late Dr. Raymond R. Lanier, who was fatally injured in an automobile accident while hunting in northeastern Colorado last fall. Appointed professor and head of the department of pathology is Dr. Morgan Berthrong, pathologist at the Glockner–Penrose Hospital in Colorado Springs since 1954. He succeeds Dr. James B. McNaught, who voluntarily stepped down as department head, a position he has occupied since August, 1945. Dr. McNaught, who has headed the American Board of Pathology, will remain on the faculty, as a professor of pathology. Dr. Conrad M. Riley, associate professor of pediatrics, Columbia University College of Physicians and Surgeons, New York City, will serve as full-time chief of Pediatric Service at Denver General Hospital, with the rank of professor of pediatrics at the C. U. School of Medicine.

ILLINOIS

Chicago

Sports Medicine Congress at Pan American Games.—A Sports Medicine Congress will be held in conjunction with the third Pan American Games, scheduled for Chicago Aug. 27-Sept. 7. The congress will meet on the Chicago campus of Northwestern University Sept. 1-2, and will feature experts in athletic training, care of injuries, diet, cardiovascular effects of sports activity, and other facets of the sports medicine field. Dr. Theodore R. Van Dellen is general chairman of the congress. Dr. Paul Dudley White, Boston, will be the featured speaker at the first plenary session Sept. 1. On Sept. 2, Dr. Allan J. Ryan, Meridian, Conn., will be the speaker. All sessions of the congress will be open to persons interested in the field of sports medicine. Information can be obtained from Dr. Van Dellen at Pan American Games, Inc., 310 S. Michigan Ave., Chicago 4.

Society News.—At the annual meeting of the Chicago Neurological Society held May 12, the following officers were elected: president, Dr. Meyer Brown; vice-president, Dr. Vladimir G. Urse; secretary, Dr. Ernst Haase; and councilor, Dr. John J. Madden.——At the annual meeting of the Metropolitan Dermatological Society of Chicago May 13 the following officers were elected: Dr. Theodore K. Lawless, president; Dr. John A. Guerrieri, vice-president; and Dr. Tibor Benedek, secretary-treasurer.

Hospital News.—Dr. Emil D. W. Hauser, associate professor of orthopedic surgery, Northwestern University Medical School, was installed as president of the medical staff of Passavant Memorial Hospital at the staff's annual meeting. He succeeds Dr. Clifford J. Barborka. Dr. Hauser has been associated with Passavant since he joined the Northwestern faculty in 1930.——The Grant Hospital of Chicago announced the inauguration of a full program of progressive patient care, with the organization of hospital facilities, services, and staff centered around the medical and nursing needs of the patients. An intensive care unit is designed for critically ill and post-operative patients, the intermediate

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

care unit for patients needing standard care, and the self-care unit for ambulatory patients.—Dr. George J. Rukstinat was elected president of the medical staff of Holy Cross Hospital at its recent annual business meeting. Dr. Rukstinat succeeds Dr. Edward J. Krol, who served as president for the past two years.

MASSACHUSETTS

Civil War Mortar Explodes.—The Springfield *Republican* for June 7, reported that Marine Sergeant Ernest Castro, of Russell, lost both arms when a Civil War mortar exploded at Eastover. The sergeant and a resort owner had fired the old weapon earlier as part of an entertainment program. The mortar misfired during a second attempt.

Dr. Schall Retires.—Dr. LeRoy A. Schall will retire from Harvard University Aug. 31, to become Walter A. LeCompte Professor of Otology and Professor of Laryngology, Emeritus. Simultaneously, Dr. Schall will retire as chief of otology and laryngology at the Massachusetts Eye and Ear Infirmary and the Massachusetts General Hospital. Dr. Schall has served the hospitals for 36 years and the Harvard Medical School for 20 years.

Personal.—Dr. C. Sidney Burwell, on Aug. 31, will become Levine Professor of Medicine, Emeritus, at Harvard, bringing to a close 40 active years of academic life. Simultaneously, he will retire as physician to the Peter Bent Brigham Hospital and as visiting physician at the Boston Lying-in-Hospital. Following his official retirement, Dr. Burwell plans to occupy an office in the Administration Building of the Medical School, where he will engage in writing the history of the Harvard Medical School. —Dr. James M. Faulkner, of Brookline, medical director, Massachusetts Institute of Technology, was elected chairman of the Joint Administrative Board of the newly formed Boston University–Massachusetts Memorial Hospitals Medical Center.

Dr. Fitzpatrick Named Wigglesworth Professor.—Dr. Thomas B. Fitzpatrick, Portland, Oregon, was appointed Edward Wigglesworth Professor of Dermatology and head of the department at Harvard Medical School, Boston. He will serve simultaneously as chief of the dermatological service at the Massachusetts General Hospital. Dr. Fitzpatrick has been on leave-of-absence at Oxford University, England, from his post as Head of the Division of Dermatology at the University of Oregon.

MICHIGAN

Society News.—The following officers were elected to serve the Western Michigan Pediatric Society during the fiscal year 1959-1960: president, Dr. Clarence L. Hoogerland, Alma; president-elect, Dr. Sprigg Jacob, Lansing; secretary-treasurer, Dr. Jerome E. Webber, Grand Rapids; and assistant secretary-treasurer, Dr. Marshall J. Feeley, Benton Harbor.—Dr. John W. Rebuck, is the president-elect of the Michigan Pathological Society. Dr. Albert F. De Groat, director of the pathology department at Herman Kiefer Hospital, is president of the society for 1959. Dr. Viola G. Brekke, pathologist for Highland Park General Hospital, remains in her capacity of secretary-treasurer.

NEW YORK

Dr. Gillies Named Division Chairman.—Dr. Alastair J. Gillies, of New Haven, Conn., became professor of anesthesiology and chairman of the Division of Anesthesiology, University of Rochester Medical Center, in July succeeding Dr. David V. Thomas. Dr. Gillies also will be anesthetist-in-chief. Since 1955, Dr. Gillies has been at the Yale University School of Medicine as assistant professor of anesthesiology and associate director of the department of anesthesia in the Grance–New Haven Community Hospital in New Haven.

Society News.—At the May 16 meeting of the Northeastern New York Radiological Society the following officers were elected for 1959-1960: president, Dr. Sidney I. Etkin, Albany; vice-president, Dr. Everett A. Jacobs, Hudson; and secretary-treasurer, Dr. Irving VanWoert Jr., Albany.—The New York Roentgen Society has appointed the following officers for the coming year: president, Dr. Harold G. Jacobson; vice-president, Dr. Frank J. Borrelli; secretary, Dr. William B. Seaman; treasurer, Dr. Albert A. Dunn; and member of executive committee, Dr. John A. Evans. All are from New York City.

New York City

Dr. Breinin Appointed Department Chairman.—Dr. Goodwin M. Breinin was appointed professor and chairman of the department of ophthalmology, New York University–Bellevue Medical Center. He was also appointed director of the eye services of University and Bellevue hospitals and consultant to the New York Veterans Administration Hospital. He succeeded Dr. Arthur G. DeVoe, who became chairman of the department of ophthalmology at Columbia University College of Physicians and Surgeons. Dr. Breinin is the first incumbent of the Daniel B. Kirby professorship of research ophthalmology at the Medical Center and he will continue to hold that professorship. In 1959 he was the recipient of the Edward Lorenzo Holmes Award of the Institute of Medicine of Chicago.

Personal.—Dr. Harry E. Ungerleider, cardiologist, was appointed consulting medical director of North American Reassurance Company. Dr. Ungerleider since 1947 had been medical director of research of The Equitable Life Assurance Society of the United

States.—Dr. Paul Klemperer, retired director, department of pathology, Mount Sinai Hospital, received on June 12 an honorary doctor of science degree at the University of Chicago with the following citation: "Devoted scholar and inspiring teacher whose discerning observations and penetrating comprehension have led to great progress in the understanding of rheumatic disease."—George T. Mills, Ph.D., of Glasgow, Scotland, was named associate professor in the department of medicine, at the State University of New York Downstate Medical Center, Brooklyn. Evelyn E. B. Smith, Ph.D., who has been working in the department of biochemistry at the University of Glasgow as a senior fellow of the Carnegie Institution of Washington was named to the post of assistant professor of medicine.

NORTH CAROLINA

Training for Medical Secretaries.—A new training program in medical secretarial work began July 1 at the Duke University Medical Center, Durham. The one-year program will combine classroom study with supervised on-the-job training. A pilot group of four students will be trained during the first year and present plans call for increasing this number to eight in 1960-1961. Participants will do classroom work in medical terminology, public relations, and general office practices. Their on-the-job training will be supervised by Duke medical secretarial personnel. Entrance requirements for the program include two years of post-high school secretarial training, either in college or business school. Students will receive a small salary to be applied toward living expenses, and certificates will be awarded upon successful completion of the program.

OHIO

Dr. Sabin Receives Science Award.—Dr. Albert B. Sabin, professor of research pediatrics, University of Cincinnati College of Medicine, on June 29 was presented with the Howard Taylor Ricketts Award of the University of Chicago "for a basic contribution to science." The presentation was made by Dr. Lowell T. Coggeshall, dean of the division of biological sciences at the university. Dr. Sabin spoke to a medical audience on the present status of the oral vaccine which he has developed. The vaccine is being used for inoculations in Russia, and mass use of the vaccine also has taken place in Mexico, Singapore, and European countries.

Fellowships for Heart Research.—Applications for heart research fellowships at Central Ohio institutions are being accepted by the Central Ohio Heart Association. To qualify, an applicant must hold a doctor's degree from an approved medical or graduate school and have served one year of internship or the equivalent. In exceptional cases, a fellowship may be awarded to an individual with a bachelor's or master's degree who has demonstrated "unusual promise." Qualified nonmedical personnel will be given equal consideration provided their projects are related to cardiology. Both clinical and basic science fellowships will be awarded for one year at an annual stipend ranging from $2,800 to $8,000. Fellows will spend full time in their research and associated studied, and clinical fellows will not be permitted to have responsibility for the care or treatment of patients, participate in resident rotation, or render hospital services customarily performed by residents. A fellow may pursue part-time studies toward a graduate degree, with prior approval of all concerned. An applicant should have a definite research program in mind, and it must be a project of which he is the senior author and is primarily responsible. He should obtain approval and make plans with an investigator under whom he is to work. The Donald Mahanna Fellowship will be awarded to an individual with an M.D. or Ph.D. who has established himself in research. It will be awarded at the discretion of the association's Fellowship Committee only when there is a candidate with "suitably superior qualifications." All applications must be postmarked not later than Sept. 15. Notification of action will be made by Dec. 1 for fellowships starting July 1, 1960. Requests for application forms should be directed to the Central Ohio Heart Association, 50 E. Broad St., Columbus 15, Ohio.

PENNSYLVANIA

Philadelphia

University News.—The senior class of the Temple University School of Medicine presented a portrait of Dr. W. Emory Burnett, chairman, department of surgery, to the Medical School. Presentation remarks by President Robert L. Johnson and an address by Dr. I. S. Ravdin, John Rhea Barton Professor of Surgery at the University of Pennsylvania, highlighted the event.—At the annual meeting of the members of the Philadelphia College of Pharmacy and Science March 23, Ivor Griffith, Ph.D., was reelected president for the 19th consecutive year. He remains as dean of the faculty, an office he has held since 1937.

WYOMING

Dedicate Rehabilitation Center.—Dedication of the new 2-million-dollar Gottsche Rehabilitation Center and Hot Springs County Memorial Hospital at Thermopolis was held June 27. Principal speaker was Dr. Frank H. Krusen, of Mayo Clinic, Rochester, Minn., who discussed "The Future of Physical Medicine and Rehabilitation." Introductory remarks were made by Mr. Charles M. Smith, Thermopolis, president of the Gottsche Foundation. Former Wyoming Governor Milward Simpson, of Cody, director of the foundation, presided at the dedication. Other speakers were Wyoming Governor J. J. Hickey; Dr. Benjamin Gitlitz, Thermopolis, president of the Wyoming State Medical Society; Mr. J. O. Spangler, Greybull, representing the Elks Lodge; and Dr. Charles H. Flint, executive director of the Gottsche Rehabilitation Center. A fund for the construction of this medical center was started in 1954. As a result of the death of their daughter, Marguerite, from poliomyelitis, William H. and Carrie Gottsche of Rock Springs, Wyo., resolved that there would be a place in the state of Wyoming to care for other persons so afflicted. Thermopolis was selected as the site. The Gottsche Foundation, a Wyoming corporation with the purpose of rehabilitation of handicapped persons, was started in a trust set up by the Gottsche family. The board decided on a plan for a combined county hospital and rehabilitation center and this plan was submitted to the voters of Hot Springs County. The hospital unit is complete with operating rooms for emergency and elective surgical procedures. In all there will be 54 beds for surgical, medical, and chronically disabled patients. The Rehabilitation Center has six treatment booths for physical therapy, two gymnasiums, occupational therapy facilities for partially disabled persons, domiciliary care units for 24 children and two housemothers, classrooms, and speech-therapy and other facilities. The Wyoming Society for Crippled Children and Adults will occupy quarters in the center.

Personal.—Dr. James W. Sampson, of Sheridan, was appointed by the Wyoming State Board of Health as director of the Department of Public Health July 1, succeeding Dr. Franklin D. Yoder, who has become director of the Division of Socio-Economic Activities of the American Medical Association.

GENERAL

Cardiology Meeting in Philadelphia.—The American College of Cardiology will hold its eighth interim meeting at the Benjamin Franklin Hotel, Philadelphia, Oct. 23-25, according to Dr. Gabriel F. Greco, Ozone Park, N. Y., member of the publication committee. This year for the first time the scientific sessions of the college will be concurrent with the 32nd annual meeting of the American Heart Association and will include a joint program. The college will conduct fireside conferences on the evening of Oct. 23, in which A. H. A. members will participate jointly. On Oct. 25, a panel on cardiac resuscitation will be presented jointly by the college and the association's council on clinical cardiology. Programs may be obtained from Dr. Philip Reichert, executive director, A. C. C., Empire State Building, New York City.

Postgraduate Medical Cruise.—The New York State Academy of General Practice will sponsor a scientific cruise to the West Indies Oct. 22-Nov. 4, aboard the liner Kungsholm, of the Swedish American Line. The scientific program will include an intensive course on hypnosis covering the use of hypnosis in general practice, anesthesiology, obstetrics and gynecology, and other medical specialties. Instruction will include practical applications in the field of general practice. The second section of the program will include selected topics in metabolism and endocrinology and the faculty will be drawn from the Albany Medical College under supervision of Dr. Frank M. Woolsey Jr., associate dean and director of postgraduate education, Albany Medical College. The program is acceptable for 18 hours of category I credit. There is no registration fee. For information, write Dr. Seymour Fiske, Chairman, Post Convention Cruise Committee, 150 E. 71st St., New York 21.

Professor Erich Hoffmann Dies.—Prof. Erich Hoffmann, an honorary member of the American Medical Association, who was associated with F. R. Schaudinn in the discovery of *Treponema pallidum,* died in Bonn, Germany, May 13, soon after celebrating his 91st birthday. Born on April 25, 1868, Professor Hoffmann was educated at Kaiser Wilhelm Academy, Berlin. He graduated in medicine in 1892, entered army medical services in 1893, and five years later became a staff officer of the Military Medical Academy in Berlin. In 1900 he obtained an appointment under Edmund Lesser in Berlin, and began to specialize in dermatology and syphilology. In 1908, Professor Hoffmann was appointed to a teaching post at the university clinic for skin diseases in Halle becoming its director a year later. In 1910 he was appointed director of the university skin clinic in Bonn and was promoted to the chair in 1918. He retired in 1934 but continued his researches for some years afterwards.

Guide for Hospital Training Programs.—"Staphylococcal Disease: Guide for Organizing Hospital In-Service Training Programs" has been produced by the U. S. Public Health Service's Communicable Disease Center, Atlanta, Ga., and is available to assist hospitals in the control of hospital-acquired staphylococcal infections. The guide was developed as a result of a recommendation of the National Conference on Hospital-Acquired Staphylococcal Disease in September, 1958, that educational programs be held by hospital infections committees for all hospital personnel. It is based on the experience acquired by the Communicable Disease Center since that time in assisting hospitals to develop such training activities. The guide has been approved by the American Hospital Association. Single copies will be distributed to state and local health departments and to more than 6,000 hospitals throughout the country. Additional copies may be obtained from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., at a charge of 30 cents each.

Physical Impairments.—The *Science News Letter* for June 27 has reported that Americans suffer from "impairments"—deafness, blindness, speech defects, cerebral palsy, and loss or absence of hands and feet—at a rate of some 141 per 1,000. This is a total of 24,000,000 impairments. Almost six Americans in 1,000 cannot read a story in an ordinary newspaper, even with the help of glasses. Another 2,000,000 Americans, more than 12 per 1,000, have visual impairments less severe than blindness. About one person in 2,000 is totally deaf, while other hearing impairments affect some 33.9 Americans in 1,000. This report, from a series on the nation's health published by the Public Health Service, points to the increasing number of older persons with impairments of some kind. In persons 75 years old or older these defects were about 12 times greater than the number found in persons under 25 years of age. Servicemen and persons in mental and other long-term institutions were not included in the survey which covered the period July, 1957, through June, 1958.

Director for Committee of World Association.—At the 12th annual meeting of the board of directors, World Medical Association, United States Committee, Inc., Mr. Henry S. McNeil, president of McNeil Laboratories, Inc., was unanimously elected to serve as a director for the term 1959-1962. The board of directors established an "Honorary Board Membership" classification for which members of the board "who have served diligently and have made distinguished contributions to the activities of the United States Committee" are eligible for election. Mr. Robert Lincoln McNeil, chairman of the board, McNeil Laboratories Inc., a member of the Board of Directors, World Medical Association, United States Committee, Inc., since its organization in 1948, was unanimously elected the first Honorary Board Member. The following were reelected officers of the board for 1959-1960: chairman, Dr. Austin Smith, president, Pharmaceutical Manufacturers Association; vice-chairman, Mr. H. J. Loynd, president, Parke Davis & Company; and secretary-treasurer, Dr. Louis H. Bauer, Secretary General, World Medical Association.

Council on Youth Fitness.—The third annual meeting of the President's Council on Youth Fitness with the President's Citizens Advisory Committee on the Fitness of American Youth will be held Sept. 13-15, at the United States Air Force Academy, Colorado Springs, Colo., Secretary of the Interior Fred A. Seaton, chairman of the council, announced. The President's Council on Youth Fitness is composed of seven Cabinet members (Interior; Defense; Agriculture; Commerce; Labor; Health, Education, and Welfare; and Housing and Home Finance Agency) charged with the responsibility of promoting the "efficacy of existing programs and the launching of additional programs which will enhance the fitness of American youth." The council seeks to "coordinate, stimulate, and improve not only the functions of federal agencies with respect to the fitness of youth, but chiefly to encourage the extension and implementation of existing local community programs by making maximum use of all facilities and organizations already in existence." The first annual meeting of the council and the advisory committee was held at the United States Military Academy, West Point, N. Y., September, 1957.

Portuguese Physician Awarded Fellowship.—The creation of the Pfizer Fellowship in Physical Medicine and Rehabilitation for a Portuguese physician to undertake postgraduate training in the United States was announced simultaneously in Lisbon and New York. The announcement in Lisbon was made by the American Ambassador of the United States to Portugal, the Hon. C. Burke Albrick. In New York, the announcement was made by Dr. Howard A. Rusk, president, World Rehabilitation Fund, Inc. The fellowship will provide a three-year period of training in physical medicine and rehabilitation for a physician from Portugal. Ambassador Albrick announced that Dr. Maria da Graca de Campos Andrada, of Lisbon, has been selected by the World Rehabilitation Fund as the Pfizer Fellow. Dr. Andrada will begin her training program in the United States at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, in July. The fellowship was made possible by a contribution to the World Rehabilitation Fund by Chas. Pfizer & Co., Inc. The fellowship will be administered by the World Rehabilitation Fund, an American voluntary organization, in cooperation with the International Society for the Welfare of Cripples.

Meeting on Biological Photography.—Newly developed uses of medical and scientific photography will be keynoted at the 1959 annual meeting of the Biological Photographic Association, to take place Aug. 31-Sept. 3 at the Sheraton Mount Royal Hotel in Montreal. This marks the first time the association will hold its annual meeting outside the United States since it was founded at Yale University in 1931. Speakers during the four-day program will describe research and administrative developments in the use of photography and motion pictures at their particular medical and dental schools, hospitals, research institutions, or science centers. Winners of the distinguished annual awards of the association will be announced in the photographic categories of clinical photography, gross specimens, photomicrographs, photomacrographs, and natural science. Motion picture awards will be announced in the categories of professional, institutional, and sequence films. Color and monochrome entries will be on display throughout the meeting, and motion pictures will also be programmed. The Biological

Photographic Association, dedicated to the skills of medical and scientific photography, has a worldwide membership which includes physicians, medical editors, educators in the fields of medicine and science, and staff photographers of medical and scientific institutions.

Surgeons to Meet in Chicago.—The 24th annual congress of the North American Federation, International College of Surgeons, will be held in the Palmer House, Chicago, Sept. 13-17. The North American Federation covers the United States, Canada, Mexico, Cuba, Haiti, Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, and Panama. Dr. Karl A. Meyer, of Chicago, and Dr. W. Wayne Babcock, of Philadelphia, have been named honorary chairmen of the congress, and Dr. Alexander Brunschwig, of New York City, has been chosen general chairman. Surgical specialties to be represented are: coloproctologic, neurologic, obstetric and gynecologic, ophthalmologic, otorhinolaryngologic, orthopedic, plastic and reconstructive, traumatic and rehabilitation, and urologic. There will be surgical motion pictures, reports on advances in military medicine, and a surgical nurses' program. The congress will be held in honor of the Chicago Medical Society and in memory of Drs. John B. Murphy, Christian Fenger, and Nicholas Senn, Chicago pioneers in surgery. Dr. Edward L. Compere, of Chicago, is president of the United States Section and secretary of the North American Federation, and Dr. Ross T. McIntire, of Chicago, is executive director of the College. Surgeons desiring to present papers should write to Dr. Peter A. Rosi, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

Society News.—At the 12th annual meeting of the board of directors of the **World Medical Association, United States Committee, Inc.**, Mr. Henry S. McNeil, president of McNeil Laboratories, Inc., was unanimously elected to serve as a director for the term 1959-1962. The following were reelected officers of the board for 1959-1960: chairman, Dr. Austin E. Smith, president, Pharmaceutical Manufacturers Association; vice-chairman, Mr. Harry J. Loynd, president, Parke Davis & Company; and secretary-treasurer, Dr. Louis H. Bauer, secretary general, World Medical Association.——At the annual meeting of the **American Radium Society** the following officers were elected for the year 1959-1960: president, Dr. Theodore R. Miller, New York City; president-elect, Dr. Jesshill Love, Louisville, Ky.; first vice-president, Dr. Gray H. Twombly, New York City; second vice-president, Dr. Leonidas D. Marinelli, Chicago; secretary, Dr. Robert L. Brown, Emory University, Ga.; and treasurer, Dr. Gilbert H. Fletcher, Houston, Texas. The 42nd annual meeting will be held at the Caribe Hilton, San Juan, Puerto Rico, March 17-19, 1960.——Dr. Booker T. Holmes, Frankfort, Ky., was named president-elect of the **John A. Andrew Clinical Society.** Dr. John W. Chenault, Bradenton, Fla., will serve as president for 1960, succeeding Dr. James D. Merida, Cleveland. Dr. Eugene H. Dibble Jr. was reelected secretary and Mr. Louis A. Rabb was elected treasurer.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	June 27, 1959		June 26, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	2
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	1	2	2
New Jersey	..	2	3
Pennsylvania	..	..	..
East North Central States			
Ohio	2	4	..
Indiana	3	5	..
Illinois	..	..	1
Michigan	2	6	4
Wisconsin	..	..	..
West North Central States			
Minnesota	1	1	..
Iowa	2	11	2
Missouri	..	5	..
North Dakota	..	..	..
South Dakota	..	..	1
Nebraska	5	6	..
Kansas	1	2	..
South Atlantic States			
Delaware	1	1	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	1	2	2
West Virginia	1	1	1
North Carolina	3	3	1
South Carolina	1	3	..
Georgia	2	2	4
Florida	..	5	3
East South Central States			
Kentucky	..	..	3
Tennessee	3	4	1
Alabama	5	5	..
Mississippi	1	7	1
West South Central States			
Arkansas	5	5	..
Louisiana	3	5	2
Oklahoma	1	4	1
Texas	13	15	20
Mountain States			
Montana	..	..	1
Idaho	..	2	..
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	..	..	2
Arizona	4	6	1
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	1
Oregon	2	2	1
California	2	3	8
Alaska	..	..	..
Hawaii	..	..	..
Puerto Rico	..	..	..
Total	65	119	68

Decrease in Marriages.—Marriages in the United States decreased by about 4% in 1958, the second straight year of decline, it is reported by statisticians of the Metropolitan Life Insurance Company. The actual number of marriages during the year was about 1,456,000 compared with 1,518,000 in 1957 and 1,585,000 in 1956. The 1958 marriage rate—8.4 per 1,000 population, including Armed Forces overseas—was the lowest recorded since 1932. Apparently, the decrease in marriages was related to business recession, the statisticians point out, since the sharpest decrease occurred in the period from September, 1957, through March, 1958. Data available thus far in 1959 indicate a small increase over the corresponding period of 1958. The annual number of marriages reportedly should climb after the early 1960's and remain at high levels for many years. There were wide geographic variations in the trend of marriages from 1957 to 1958, with 26 states showing decreases and 22 states and the District of Columbia having increases. The sharpest decreases were in those states with changes in their marriage laws, while adjoining states had the biggest increases. Indiana, where a waiting period has been required since January, 1958, had the biggest drop —45%. Marriages in the adjoining states of Ohio and Kentucky increased by 10% and 23%, respectively. In Mississippi, where the legal age for marriage was raised on July 1, 1958, marriages decreased by 42%. Among cities with at least one million population, Los Angeles alone showed no change. New York had a 3% decrease, Chicago and Philadelphia had 4% decreases, and Detroit almost 7%. Alaska and Hawaii, included in the United States record, had respectively a 3% increase and a 3% decrease in marriages.

CANADA

Symposium on Urethritis and Trichomoniasis.—The first Canadian Symposium on Non-Gonococcal Urethritis and Human Trichomoniasis will be held Sept. 21-22 at Notre Dame Hospital, Montreal, under the patronage of the Honorable Waldo J. Monteith, minister of national health and welfare, and Dr. Arthur J. B. Leclerc, minister of health of the Province of Quebec. Several European and American physicians will participate, including Dr. Pierre Durel, of Paris, chairman, International Study Group on Human Trichomoniasis; Dr. Gaston Chappaz, professor of gynecology, University of Reims; Dr. Ambrose J. King, director, Whitechapel Special Clinic; and Dr. Louis G. Feo, of the department of gynecology and obstetrics, Jefferson Medical College of Philadelphia. Interested physicians are invited. For information, write Dr. Zoltan Gallai, secretary of the symposium, 8580 Esplanade Ave., Montreal 11, Quebec, Canada.

FOREIGN

Meeting of French-Speaking Pediatricians.—The 17th Congress of the French-Speaking Society of Pediatrics will take place Oct. 12-14 at Montpellier, France, under the presidency of Prof. Jean Chaptal. Subjects include the following:

Hypoparathyroidism in Nurslings and Children.
Neonatal and Childhood Icterus.
Physiological and Pathological Aspects on Electroencephalography in the Course of Cerebral Maturation.

For information concerning the congress write Prof. Jean Chaptal, General Secretary of the Congress, 8, rue Guillaume-de-Nogaret, Montpellier, France.

Congress on Chest Diseases.—The sixth International Congress on Diseases of the Chest, sponsored by the American College of Chest Physicians, will be held at the University of Vienna from Aug. 28 to Sept. 1, 1960, organized by medical societies of Austria. The program includes problems connected with the physiology, pathology, clinical aspects, and therapy of the diseases of the organs of the chest in the adult and in the child. Scientists, clinicians, and practitioners from all parts of the world will attend. It is intended to have simultaneous interpretation of the papers in English, French, German, Russian, and Spanish. For information, write Prof. Dr. A. Sattler, Generalsekretar, American College of Chest Physicians, Wien IX, Frankgasse 8, Austria.

Meeting of Cardiovascular Society in Munich.—The fourth International Congress of the International Cardiovascular Society will be held Sept. 18-20 in Munich, Germany, at Das Deutche Museum, under the presidency of Dr. Michael E. DeBakey, Houston, Texas. A cardiovascular forum, Sept. 18, will be a joint session with the International Society of Surgery. A symposium on arterial grafts will be held Sept. 19, and a symposium on open heart surgery, Sept. 20. A program of motion pictures on cardiovascular problems is planned. Simultaneous translation in English, French, German, and Spanish will be available for all presentations. Technical exhibits will be on display. For information, write Dr. Henry Haimovici, 715 Park Ave., New York 21, Secretary-General.

CORRECTION

Foundation for Medical Care.—In the italicized introduction to a paper on this subject in the Council on Medical Service section in THE JOURNAL, June 20, 1959, page 969, it was stated that the Los Angeles County Medical Association is the most recent medical society to approve the formation of such a foundation. The executive director of the Los Angeles County Medical Association writes that this statement is erroneous to this degree:

> The Council of the Los Angeles County Medical Association, which is its sole policy body, has not taken any official action regarding the approval of a Foundation for Medical

Care. In January, the Council authorized a postcard opinion-poll of the membership of LACMA, to see whether there was any interest in the formation of a Foundation. Following this, the Council of LACMA instructed its Medical Services Committee to make preliminary studies and conduct some hearings and find out more about the Foundation, and to date there has been no final report on the Foundation, and the Council has not taken any official action.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications was June 22. Succeeding examinations—March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23, 1960. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Examination.* Phoenix, Oct. 14-16. *Reciprocity.* Phoenix, Oct. 17. Ex. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

Arkansas:* *Examination and Reciprocity.* Little Rock, Nov. 5-6. Sec., Dr. Joe Verser, Harrisburg.

California: *Written.* Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Connecticut:* *Homepathic. Examination.* Derby, Sept. 8. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

District of Columbia:* *Examination.* Washington, Dec. 14-15. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Florida:* *Examination.* Miami Beach, Nov. 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, Oct. 13. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity.* Kansas City, January 1960. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Louisiana: *Examination and Reciprocity.* New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maryland: *Examination.* Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination and Endorsement.* Boston, July 14-17. Sec., Dr. David W. Wallwork, Room 37, State House, Boston 33.

Montana: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

Nevada:* *Examination and Reciprocity.* Reno, Sept. 8. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

New Hampshire: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

New Jersey: *Examination.* Trenton, Oct. 20-23, *Reciprocity.* Monthly, Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

New Mexico:* *Examination and Reciprocity:* Santa Fe, Nov. 16-17. Sec., Dr. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination.* Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

Ohio: *Examination.* Columbus, Dec. 15-17. *Endorsement.* Columbus, Aug. 26 and Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

Puerto Rico: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Tennessee:* *Examination.* Memphis, Sept. 23-24. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

Texas:* *Examination.* Fort Worth, Dec. 3-5. *Reciprocity.* Houston, Aug. 29-31. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 5. Sec., Dr. James W. Shannon, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination and Reciprocity.* Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

Arizona: *Examination.* Tucson, Sept. 15. Sec., Mr. Herman E. Bateman, University of Arizona, Tucson.

Colorado: *Examination.* Denver, Sept. 2-3. *Reciprocity.* Denver, Sept. 4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, Oct. 10. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

District of Columbia: *Examination.* Washington, Nov. 23-24. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Kansas: *Examination.* Pittsburg, Nov. 6-7. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 9-10. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Minnesota: *Examination.* Minneapolis, Oct. 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

Oklahoma: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

South Dakota: *Examination.* Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Texas: *Examination.* Austin, Oct. 12-13. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 11 and Milwaukee, Dec. 5, Sec., Mr. Wm. H. Barber, 621 Ranson St., Milwaukee.

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*Basic Science Certificate required.

DEATHS

Amerson, Simeon Smith, Georgetown, Ky.; University of Nashville (Tenn.) Medical Department, 1897; served as president of the Scott County Medical Society; died in the John Graves Ford Memorial Hospital May 2, aged 90.

Antoni, Adolph I., Norwalk, Conn.; Boston University School of Medicine, 1927; associated with the Norwalk Hospital, where he died May 2, aged 57.

Arnett, John Hancock Jr., Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1948; interned at the Cambridge City Hospital in Cambridge, Mass., and served a residency at the Harrisburg (Pa.) State Hospital; associated with the Mayview (Pa.) State Hospital; died May 7, aged 33.

Asa, Athenus Lewis, Morrill, Neb.; Lincoln Medical College of Cotner University, 1906; died in the West Nebraska General Hospital, Scottsbluff, March 8, aged 79.

Barnette, Ortha James, Shreveport, La.; Louisiana State University School of Medicine, New Orleans, 1952; interned at Charity Hospital of Louisiana in New Orleans, where he served a residency; served in the medical corps of the U. S. Naval Reserve; on the staffs of the T. E. Schumpert Memorial Sanitarium and the Physicians and Surgeons Hospital; died Feb. 7, aged 29.

Bennett, William Lewis Ⓜ Burnsville, N. C.; Lincoln Memorial University Medical Department, Knoxville, Tenn., 1911; member of the state legislature for two years; died in St. Joseph's Hospital, Asheville, April 30, aged 75.

Bingaman, Dixi McLean Ⓜ Salinas, Calif.; University of Southern California School of Medicine, Los Angeles, 1939; died April 28, aged 48.

Bowdoin, William Henry, Statham, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1913; died April 28, aged 79.

Braun, Eugene J. Ⓜ New York City; Universita Karlova Fakulta Lékarskà Praha, Czechoslovakia, 1932; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; interned at the Metropolitan Hospital in New York City, where he served a residency; served a residency at the Brooklyn State Hospital and the Central Islip (N. Y.) State Hospital; served on the staff of the Hillside Hospital; died May 7, aged 51.

Calonge, Guy Earl Ⓜ La Junta, Colo.; born in 1892; Loyola University School of Medicine, Chicago, 1918; served as secretary of the Otero County Medical Society of which he was president three times and one of the founders; formerly vice-president of the Colorado State Medical Society; member of the American Trudeau Society and the American Academy of General Practice; served three terms as a member of the District II School Board and as a member of the city council; his community efforts were recognized in 1954 when he received the third Civic Service Award of the Chamber of Commerce, of which he was a life member, and the naming of a building at Otero Junior College, Calonge Hall; veteran of World War I; associated with Mennonite Hospital and Santa Fe Hospital; died April 29, aged 66.

Castro, Cosimo Ⓜ Park Ridge, Ill.; Loyola University School of Medicine, Chicago, 1930; veteran of World War II; interned at Columbus Hospital in Chicago; associated with the Veterans Administration in Chicago, where he was adjudication officer at West Side Regional Office; in 1954, on 25th anniversary of graduation, he was cited for outstanding contributions as an alumnus by Stritch School of Medicine of Loyola University; died May 1, aged 60.

Chepko, Milan Daniel, Lyons, Ohio; Hahnemann Medical College and Hospital of Philadelphia, 1946; veteran of World War II; interned at the Easton (Pa.) Hospital and the Community General Hospital in Reading, Pa.; died in Flower Hospital, Toledo, April 29, aged 36.

Colburn, Charles Robert, Fairborn, Ohio; Eclectic Medical College, Cincinnati, 1927; died in the Community Hospital, San Bernardino, Calif., April 11, aged 64.

Collins, William Thomas, Albuquerque, N. M.; Northwestern University Medical School, Chicago, 1909; died in Fort Lyon, Colo., April 22, aged 75.

Davies, William Ⓜ Lyons, Ill.; Northwestern University Medical School, Chicago, 1924; member of the American Academy of General Practice; associated with the MacNeal Memorial Hospital in Berwyn, where he died April 19, aged 78.

Dean, Wesley N. Ⓜ Boyd, Texas; Baylor University College of Medicine, Dallas, 1901; for many years health officer; past-president of the Rusk County Medical Society; died in Overton (Texas) Hospital April 17, aged 90.

Ⓜ Indicates Member of the American Medical Association.

Dix, Sherwood, Largo, Fla.; Maryland Medical College, Baltimore, 1902; veteran of World War I; served on the staffs of various Veterans Administration hospitals; died in the Morton Plant Hospital, Clearwater, April 21, aged 85.

Donnell, Louis August, Wichita, Kan.; University of Louisville (Ky.) School of Medicine, 1937; served as city commissioner and mayor; veteran of World War II; on the staffs of Wesley and St. Joseph hospitals; died in Perryville, Ark., May 1, aged 53.

Doody, Richard Patrick Ⓜ Troy, N. Y.; Albany (N. Y.) Medical College, 1916; veteran of World War I; fellow of the American College of Surgeons; past-president of the Rensselaer County Medical Society; chief surgeon at St. Mary's Hospital; for many years surgeon for the police and fire departments; member of the executive board of his alma mater; past-president of the Lions Club; died May 8, aged 64.

Felsher, Wolf Zachary Ⓜ Chicago; Chicago College of Medicine and Surgery, 1917; veteran of World War I; for many years associated with the Michael Reese Hospital; civilian medical officer at the Fifth Army headquarters; died in the Grant Hospital May 9, aged 70.

Fischer, Edward James Ⓜ West Orange, N. J.; Georgetown University School of Medicine, Washington, D. C., 1922; police surgeon; associated with St. Mary's Hospital in Orange; died May 6, aged 61.

Ganley, Arthur Joseph Ⓜ East Orange, N. J.; Tufts College Medical School, Boston, 1916; veteran of World War I; associated with Presbyterian Hospital in Newark, where he died May 8, aged 70.

Hederick, Austin Ross Ⓜ Booneville, Ark.; Memphis (Tenn.) Hospital Medical College, 1902; veteran of World War I; honored in 1957 with a "Dr. Hederick Day" celebration at Booneville; for many years president of the school board; died in Newport April 25, aged 91.

Heinen, Joseph Peter, Chicago; Rush Medical College, Chicago, 1895; for many years diagnostician for the city board of health; served on the staffs of Alexian Brothers and St. Elizabeth hospitals; died May 10, aged 86.

Hindman, Thomas Audley Newcomer, Kensington, Md.; University of Pittsburgh School of Medicine, 1938; associated with Suburban Hospital in Bethesda; died April 28, aged 49.

Jameson, Winifred Mitchell Carney Ⓜ San Francisco; University of California School of Medicine, San Francisco, 1950; interned at Franklin Hospital; served a residency at the University of California Hospital and Franklin Hospital in San Francisco, and the Ernest V. Cowell Memorial Hospital in Berkeley, Calif.; resident in internal medicine at the Veterans Administration Hospital; died May 9, aged 46.

Jesion, Joseph William Ⓜ Pine River, Minn.; Milwaukee Medical College, 1912; veteran of World War I; for many years associated with the Northern Pacific Beneficial Association Hospital in St. Paul; died in the Veterans Administration Hospital in St. Cloud, April 29, aged 70.

Johannes, Richard L., Nevada, Mo.; Louisville (Ky.) Medical College, 1898; died in the Nevada Hospital April 25, aged 82.

Keller, Jacob Molier, Steeleville, Ill.; Washington University School of Medicine, St. Louis, 1904; died March 17, aged 79.

Kheiralla, George Ibrahim, Cambridge, Mass.; Northwestern University Medical School, Chicago, 1902; Chicago Homeopathic Medical College, 1900; author of "Arabia Reborn"; died April 18, aged 79.

King, Robert Rogers Ⓜ Wilkesboro, N. C.; University of Arkansas School of Medicine, Little Rock, 1906; health officer of Wilkes County; served as health officer of the district made up of Ashe, Alleghany, and Watauga counties; formerly health officer of Cherokie, Graham, and Clay counties; for many years a medical missionary for the Presbyterian Church in the Belgian Congo in Africa; died in Charlotte April 29, aged 74.

Kuhr, Ernestus Otto Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1902; died in the Roosevelt Hospital May 7, aged 81.

Leventhal, Max Ⓜ Dolgeville, N.Y.; University of St. Andrews Conjoint Medical School, St. Andrews and Dundee, Scotland, 1933; at various times health officer of the towns of Manheim, Salisbury, and Dolgeville, in Herkimer County, and the town of Stratford in Fulton County; secretary of the staff of Little Falls (N. Y.) Hospital; died in the Mary Imogene Bassett Hospital, Cooperstown, April 11, aged 52.

Lichtwardt, Hartman A., Detroit, Mich.; Detroit College of Medicine and Surgery, 1917; also ordained a Presbyterian minister; a medical missionary in Iran for many years; served as medical director of the Woman's Hospital; fellow of the American College of Surgeons; died April 28, aged 66.

Lilienthal, Walter Scott, Albany, N. Y.; Albany (N. Y.) Medical College, 1910; on the courtesy staff of Albany Hospital, where he died April 28, aged 73.

McFarlane, Carl H., Honaker, Va.; Lincoln Memorial University Medical Department, Knoxville, Tenn., 1914; died in Rosedale, April 15, aged 73.

McGhee, Moses Alfred Ⓜ Daleville, Ala.; University of the South Medical Department, Sewanee, Tenn., 1898; past-president of the Dale County Medical Association; died April 20, aged 84.

McKeown, Charles Davis Ⓜ Wichita, Kan.; Loyola University School of Medicine, Chicago, 1918; specialist certified by the American Board of Anesthesiology; member of the Aero Medical Association and the Association of Life Insurance Medical Directors of America; past-president of the Sedgwick County Medical Society; medical director of the Farmers & Bankers Life Insurance Company; in 1949 appointed to the City Planning Commission; associated with St. Francis Hospital, Wesley Hospital, and St. Joseph Hospital, where he died April 29, aged 67.

McNally, Francis Joseph Ⓜ Pompano Beach, Fla.; born in Springfield, Mass., March 1, 1919; Columbia University College of Physicians and Surgeons, New York City, 1944; certified by the National Board of Medical Examiners; interned at the Bellevue Hospital, New York City; served a residency at the Traumatic Surgery Reconstructive Unit of the New York Post-Graduate Medical School and Hospital in New York City, City Hospital in Cleveland, and the Sunny Acres, Cuyahoga County Tuberculosis Hospital in Cleveland; for two years served in the medical corps, Army of the United States; associated with North Broward General Hospital and Holy Cross Hospital in Fort Lauderdale; died April 22, aged 40.

Macrae, Donald Hanley Ⓜ Topeka, Kan.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1937; interned at the Montreal General Hospital in Montreal, Que., Canada, where he served a residency; served a fellowship at Menninger Sanatorium in Topeka and a residency at the Veterans Administration Hospital in Topeka; since 1950 county coroner; died in St. Francis Hospital April 26, aged 52.

Malbin, Barney Ivan, Portland, Ore.; Rush Medical College, Chicago, 1936; specialist certified by the American Board of Internal Medicine; served on the faculty of his alma mater; formerly associated with the Michael Reese Hospital in Chicago; veteran of World War II and received the Air Medal; on the staff of the Holladay Park Hospital; died May 4, aged 49.

Mayo, Dana Bartlett, Kennebunk, Maine; Boston University School of Medicine, 1906; past-president of the York County Medical Society; veteran of World Wars I and II; served in the U. S. Public Health Service, U. S. Judication Board, Washington, D. C., and the Veterans Administration; died April 19, aged 76.

Meboe, Joseph Ⓜ Viola, Wis.; University of Wisconsin Medical School, Madison, 1941; veteran of World War II; awarded the Purple Heart and the Bronze Star; served on the staffs of the Richland Center (Wis.) Hospital and the Vernon Memorial Hospital in Viroqua; died in La Crosse May 3, aged 48.

Mitchell, Roscoe L. Ⓜ Augusta, Maine; University of Vermont College of Medicine, Burlington, 1908; retired as director of the bureau of health in the state department of health and welfare May 1, 1947; city physician and city health officer; member of the American Public Health Association and the Maine Public Health Association; served as vice-president and executive member of the U. S. Association of State and Territorial Health Officers; physician for the Kennebec County Jail; on the staff of Augusta General Hospital, where he died April 21, aged 82.

Moore, Clyde Newton, Murrieta, Calif.; Lincoln (Neb.) Medical College, of Cotner University, 1911; served on the staff of the Community Hospital in Long Beach; died in Garden Grove, March 25, aged 77.

Munford, Raymond Hunter Ⓜ La Habra, Calif.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1907; veteran of World War I; died April 15, aged 79.

Munsell, William Marvin, Grandview, Wash.; Missouri Medical College, St. Louis, 1895; veteran of World War I; served as medical examiner for the Northern Pacific and Union Pacific railroads; died April 19, aged 87.

Murray, Louis Floyd Ⓜ St. Louis; St. Louis College of Physicians and Surgeons, 1911; served overseas during World War I; on the staff of the Lutheran Hospital, where he died April 26, aged 72.

Munzner, Ralph Ⓜ Alton, N. Y.; Hessische Ludwigs-Universität Medizinische Fakultät, Giessen, Hesse, Germany, 1923; county coroner; served with the German Army in World War I; member of the American Academy of General Practice; associated with Lyons (N. Y.) Hospital and the Myers Community Hospital in Sodus; died April 25, aged 62.

Noonan, George Matthew Ⓜ Denver; University of Pittsburgh School of Medicine, 1906; also a pharmacist; died April 20, aged 79.

Orcutt, Dwight Chapman Ⓜ Evanston, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; for many years on the staff of St. Luke's Hospital in Chicago; died in Chicago May 13, aged 86.

Opperman, Ralph Clifford, Miami, Fla.; Jefferson Medical College of Philadelphia, 1923; died April 13, aged 58.

Padykula, Stanley George Ⓜ Endicott, N. Y.; Medical College of South Carolina, Charleston, 1939; veteran of World War II; formerly member of the Union-Endicott School Board; served on the staffs of Charles S. Wilson Memorial Hospital in Johnson City and the Ideal Hospital; died May 1, aged 47.

Paepke, Paul, Milwaukee; Eclectic Medical College, Cincinnati, 1926; died in the Milwaukee Hospital April 29, aged 62.

Pendleton, George Franklin Ⓜ Kansas City, Mo.; Western Reserve University School of Medicine, Cleveland, 1914; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; on the staffs of the General and Menorah hospitals; member and past-president of the staffs of St. Mary's Hospital and the Trinity Lutheran Hospital, where he was chairman of the obstetrics department and where he died May 5, aged 75.

Philipp Von Sielentz, W. M., Great Neck, N. Y.; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1927; during World War II served as a major, medical corps, 104th Field Artillery; died April 18, aged 62.

Pierce, William Meredith Ⓜ Tuscumbia, Ala.; Memphis (Tenn.) Hospital Medical College, 1903; past-president of the Colbert County Medical Society; served in France during World War I; died April 30, aged 75.

Plummer, Albert Wyman Ⓜ Lisbon Falls, Maine; Medical School of Maine, Portland, 1894; served three terms in the state legislature; on the staff of the Central Maine General Hospital in Lewiston, where he died May 1, aged 90.

Randall, John Hammond Ⓜ Iowa City, Iowa; State University of Iowa College of Medicine, Iowa City, 1928; certified by the National Board of Medical Examiners; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; past-president of the Iowa Obstetrics and Gynecology Society; professor and head of the department of the obstetrics and gynecology, State University of Iowa College of Medicine, where he was a member of the staff since 1934; associated with University Hospital, where he died April 19, aged 60.

Ray, Claud Burton, Cassadaga, Fla.; Michigan College of Medicine and Surgery, Detroit, 1906; formerly practiced in Detroit; died in Halifax District Hospital in Daytona Beach, April 28, aged 77.

Ray, Thomas Allen, Falls Church, Va.; Johns Hopkins University School of Medicine, Baltimore, 1952; interned at the Grace-New Haven Community Hospital, New Haven Unit, New Haven, Conn., where he served a residency; veteran of World War II; associated with Georgetown Hospital in Washington, D. C., and the Arlington (Va.) Hospital; died in Washington, D. C., May 6, aged 34.

Rech, Joseph Francis Ⓜ Indiana, Pa.; Georgetown University School of Medicine, Washington, D. C., 1931; veteran of World War II; served as secretary of the Indiana County Medical Society; on the staff of the Indiana Hospital; died April 18, aged 54.

Remington, Avon Charles Ⓜ Los Angeles; Harvard Medical School, Boston, 1940; interned at the Rochester General Hospital in Rochester, N. Y.; served a residency at the New York State Psychiatric Institute and Hospital in New York City and the Compton (Calif.) Sanitarium; veteran of World War II; member of the Aero Medical Association and the Industrial Medical Association; medical director, Garrett Corporation, Air Research Division; associated with the Daniel Freeman Memorial Hospital in Inglewood; died May 6, aged 43.

Robin, Percival Albert Ⓜ Hempstead, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1932; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society; fellow of the American College of Radiology; past-president of the Radiological Society of the State of New York; associated with Nassau Hospital in Mineola, Manhasset (N. Y.) Medical Center, and the Meadowbrook Hospital in Hempstead; veteran of World War II; died April 30, aged 52.

Rollins, Wiley Jackson Ⓜ Houston, Texas; University of Virginia Department of Medicine, Charlottesville, 1925; fellow of the International College of Surgeons; member of the Industrial Medical Association; for many years on the staff of the Memorial Hospital, where he died May 2, aged 58.

Rombkowski, John Anthony Ⓜ Toledo, Ohio; Loyola University School of Medicine, Chicago, 1918; member of the American Academy of General Practice; on the staff of St. Vincent's Hospital, where he died April 14, aged 74.

Rothschild, Charles Joseph Ⓜ Fort Wayne, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1905; past-president of the Fort Wayne Medical Society (Allen County); at one time served as Allen County coroner; served as chief of staff, St. Joseph's Hospital; died April 28, aged 77.

Rousuck, A. Ashley Ⓜ Cleveland; Wayne University College of Medicine, Detroit, 1940; interned at Robert Packer Hospital in Sayre, Pa., where he served a residency; entered Mayo Foundation in Rochester, Minn., as a fellow in internal medicine in October, 1942, and left in October, 1945; on the staffs of the St. Luke's and Mount Sinai hospitals; died April 22, aged 48.

Rudie, Clifford Norman Ⓜ St. Peter, Minn.; University of Louisville (Ky.) School of Medicine, 1928; died in the Methodist Hospital, Rochester, April 16, aged 59.

Ryall, Wallace Wilberforce Ⓜ Youngstown, Ohio; Western Pennsylvania Medical College, Pittsburgh, 1897; past-president of the Mahoning County Medical Society; veteran of World War I; served as city health commissioner, member of the city board of health and the state board of health; chief examiner for the Civil Service Commission, a judge for the Boxing Commission, president of the Kiwanis Club for a term and one of its directors for many years; on the emeritus staff, Youngstown Hospital Association; died in the Sawyer Sanatorium in Marion April 25, aged 84.

Ryan, William Butler Jr., Beaufort, S. C.; Medical College of South Carolina, Charleston, 1914; veteran of World War I; on the staff of the Beaufort Memorial Hospital; died May 8, aged 67.

Ryder, Charles Ambler, Brookfield Center, Conn.; Yale University School of Medicine, New Haven, 1898; served as postmaster and as secretary of the board of education for many years; died in the Fairfield State Hospital in Newtown April 23, aged 84.

Samuel, Meredith Ivor Ⓜ Wilmington, Del.; University of Maryland School of Medicine, Baltimore, 1900; served overseas during World War I; past-president of the Medical Society of Delaware; retired from the Veterans Administration Nov. 30, 1953; chief of medical service, Delaware, St. Francis, and Wilmington General hospitals; consultant, Delaware State Hospital, Farnhurst; served as medical director of the Brandywine Sanatorium in Marshalltown; died in the Veterans Administration Hospital, Elsmere, April 22, aged 83.

Sanford, Arthur Hawley Ⓜ Rochester, Minn.; born in New Albin, Iowa, Jan. 12, 1882; Northwestern University Medical School, Chicago, 1907; from 1907 to 1911 a member of the faculty of medicine at Marquette University, Milwaukee, where he was successively assistant professor, associate professor, and professor of physiology; emeritus member of the staff at the Mayo Clinic, where in 1911 he entered as bacteriologist, and was director of the clinical laboratories; head of the section of clinical pathology until 1946 at which time he became a senior consultant, and in 1949 retired from the clinic; emeritus professor of clinical pathology in the Mayo Foundation, Graduate School, University of Minnesota; when the foundation was established in 1915, he was appointed an associate professor of clinical pathology and parasitology; advanced to professor in 1921 and held this chair until 1950; elected first president of the American Board of Pathology, Inc., in 1936 and held this post until 1946; one of the original trustees of the board; chairman, Section on Pathology and Physiology, American Medical Association, 1929-1930; a charter member and past-president of the American Society of Clinical Pathologists, which in 1933 awarded him the Ward Burdick gold medal; in 1956 was honored at the annual meeting of the College of American Pathologists, of which he was a member, with the award of the Scientific Products Foundation, "in recognition of his outstanding service to pathology and to the field of medicine"; fellow of the American College of Physicians; member of the Minnesota State Medical Association, which elected him to the 50-year club in 1957, the American Association for the Advancement of Science, the American Society of Immunologists, the Society for Experimental Biology and Medicine, the Alumni Association of the Mayo Foundation, the Society of the Sigma Xi, Alpha Omega Alpha, Alpha Kappa Kappa, and Sigma Nu; Northwestern University conferred a distinguished service award on him in 1940; appointed an honorary consultant to the Army Medical Library in Washington, D. C.; in 1950 the board of regents of the University of Minnesota awarded him a certificate of merit for his long service to the university as a member of the faculty of the Mayo Foundation; in 1947 the Minnesota Society of Clinical Pathologists established the Arthur H. Sanford Lecture in Pathology in his honor; the lecture is given by an outstanding figure in the field at annual sessions of the Minnesota Medical Association; appointed a special consultant to the U. S. Public Health Service and a member of the advisory council on serology of that agency; member of the board of directors of the Rochester Public Library from 1914 to 1924; member of the Rochester Board of Education from 1924 to 1940 and served as president for 14 years of that time; president of the Olmsted County Historical Society from 1948 to 1950; first registered scoutmaster in Rochester and was a member of the national council of Boy Scouts of America; received a veterans' award for 40 years of service to the Boys Scouts in 1953; since 1950 director of the laboratories at the Rochester State Hospital; co-author of "Clinical Diagnosis by Laboratory Methods," the 12th edition of which appeared in 1953; died April 28, aged 77.

Sarubin, Benjamin Ⓜ Baltimore; George Washington University School of Medicine, Washington, D. C., 1927; died in the Lutheran Hospital April 23, aged 61.

Selleck, Nathaniel Benedict Ⓜ St. Petersburg, Fla.; Long Island College Hospital, Brooklyn, 1924; formerly practiced in Danbury, Conn., where he was associated with Danbury Hospital, and served as president of the Fairfield County Medical Society; died in St. Anthony's Hospital April 21, aged 60.

Shapleigh, Edward E. Ⓜ Kittery, Maine; Medical School of Maine, Portland, 1890; served as health officer and coroner for many years; died in the York Hospital, York Village, April 27, aged 91.

Shoaff, Paris Alexander Ⓜ New Castle, Pa.; Jefferson Medical College of Philadelphia, 1918; past-president of the Lawrence County Medical Society; fellow of the American College of Surgeons; associated with New Castle and Jameson Memorial hospitals; died April 22, aged 66.

Shull, Ernest Clay Ⓜ Herndon, Va.; Medical College of Virginia, Richmond, 1924; *served in France* during World War I; for many years member of the school board; past-president of the Rotary Club; associated with Loudoun Hospital in Leesburg, Arlington (Va.) Hospital, Washington Medical Center, Georgetown Hospital, and the Doctors Hospital, Washington, D. C., where he died May 7, aged 65.

Slaughter, Clarence Baden Powell Ⓜ Cleveland; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1923; veteran of World War I; died in South Euclid, Ohio, April 24, aged 58.

Smith, Adonis Ⓜ Hope, Ark.; Memphis (Tenn.) Hospital Medical College, 1904; veteran of the Spanish-American War and World War I; died in Little Rock April 22, aged 88.

Smith, Ernest Franklin, Kenton, Del.; College of Physicians and Surgeons, Baltimore, 1905; formerly executive secretary of the state board of health; served as health commissioner of Sussex County and Kent County; died April 17, aged 82.

Smith, Grace F., Chicago; Chicago College of Medicine and Surgery, 1913; died in the Englewood Hospital April 1, aged 72.

Smith, J. Russell Ⓜ Middleburgh Heights, Ohio; Western Reserve University School of Medicine, Cleveland, 1951; interned at the City Hospital in Cleveland, where he served a residency; specialist certified by the American Board of Surgery; veteran of World War II; demonstrator of surgery at his alma mater; associated with Fairview Park Hospital in Cleveland; on the staff of the Community Hospital in Berea; died April 20, aged 34.

Sothoron, Levin Johnson Ⓜ Charlotte Hall, Md.; Georgetown University School of Medicine, Washington, D. C., 1896; for many years served as school physician of Charlotte Hall Military Academy; on the staff of St. Mary's Hospital in Leonardtown; died in La Plata April 19, aged 86.

Spikes, James Lewis, Pocahontas, Ark.; University of Arkansas School of Medicine, Little Rock, 1928; died April 19, aged 57.

Staff, Edmond Peter Ⓜ Ramsey, Ill.; Missouri Medical College, St. Louis, 1895; veteran of World War I; for many years a member of the school, serving as president for 22 years; died in the Fayette County Hospital, Vandalia, April 18, aged 89.

Taylor, John Eldredge, Morganton, N. C.; Medical College of Virginia, Richmond, 1922; died in the Grace Hospital April 16, aged 68.

Vorhaus, Martin Grossman Ⓜ New York City; University Bellevue Hospital Medical College, New York City, 1918; specialist certified by the American Board of Internal Medicine; member of the American Gastroenterological Association; veteran of World War I; consultant, internal medicine, Hospital for Joint Diseases; in 1935 received a special Certificate of Merit from the American Medical Association for group exhibit for studies on crystalline vitamin B_1; author of "A Guide to General Medical Practice," "The Changing Patient-Doctor Relationship," and "Adam's Rib"; died in the Lenox Hill Hospital April 29, aged 62.

Weinstein, Adolph Joseph Ⓜ Charlotte Amalie, Virgin Islands; Long Island College Hospital, Brooklyn, 1922; specialist certified by the American Board of Otolaryngology; served on the staff of the New York Polyclinic Medical School and Hospital in New York City; on the staff of Knud-Hansen Memorial Hospital and department of health; died April 15, aged 61.

Weiss, Jacob Joseph, New York City; University and Bellevue Hospital Medical College, New York City, 1915; died in the Bronx Hospital April 21, aged 68.

Wentworth, Ernest, Limington, Maine; College of Physicians and Surgeons, Boston, 1902; died April 15, aged 85.

Wight, Bennett Allen Ⓜ Kermit, Texas; Tulane University School of Medicine, New Orleans, 1926; veteran of World War II; county health officer; member of the Kermit Chamber of Commerce; on the staff of the Winkler County Memorial Hospital, where he died April 17, aged 57.

Wohlford, Reuben Franklin Ⓜ South Charleston, W. Va.; Medical College of Virginia, Richmond, 1942; interned at Lewis-Gale Hospital in Roanoke, where he served a residency; veteran of World War II; chief of staff and past-president of staff, Herbert J. Thomas Memorial Hospital, where he died April 19, aged 45.

FOREIGN LETTERS

DENMARK

Functional Myalgias.—L. H. Leinøe (*Nord. med.* 61:609-611 [April 16] 1959) drew attention to the fact that patients with functional myalgias often had symptoms indicating dysfunction of the autonomic nervous system, such as coldness of the extremities and acrocyanosis. These patients did not seem to tolerate the usual treatment by deep heat and massage, particularly short-wave diathermy. The reason for this might be a sympathetic dominance previously shown to occur frequently in these patients. Anxiety states, psychic stress, frustration, and maladjustment lead to autonomic imbalance and vascular instability associated with ischemia, oxidative changes, and muscular spasm induced by pain. A group of 27 patients with myalgia and objective signs of autonomic dysfunction were treated with indirect heat in the form of whole-body cold packs, under the influence of which there occurred a reflex vasoconstriction of short duration, followed by maximal dilatation and warming. These patients responded well to this form of treatment. There were no untoward reactions and all became free from pain or relieved of most of their symptoms. This effect was indicative of an autonomic dysfunction in the muscles.

INDIA

Thoracoplasty and Ventilatory Functions.—Gharpure and Nigam (*Indian Journal of Surgery,* vol. 21, February, 1959) stated that the effect of thoracoplasty in patients with pulmonary tuberculosis is not limited to the healing of cavities; it may also damage the adjoining lung tissue. The thoracic cage on the side operated on becomes relatively rigid and immobile, causing diminution of respiratory excursions and ventilatory function. This is further aggravated by the deformity of the spine resulting from thoracoplasty. The authors estimated pulmonary function before and three months after thoracoplasty in 12 patients. The vital capacity was found to be uniformly lowered after the operation. No patient with a vital capacity of below 2,000 cc. was accepted for operation. The average normal values for maximum breathing capacity (MBC) in men is 150 and in women 100 liters. An MBC below 40% of the predicted value is not sufficient for daily requirements.

In two patients in this study it was lowered to 42 and 45 liters after thoracoplasty, making them more or less respiratory cripples. Two others with an MBC of 55 liters became dyspneic on walking or slight exertion. Six had an MBC of almost 100 liters before operation and these retained good ventilatory capacity even after operation. The walking dyspneic index (walking ventilation x 100/MBC) is important for assessing the degree of pulmonary insufficiency. Normally it is below 0.3. The patient is a respiratory cripple when it goes above 0.5, as it did in two patients after thoracoplasty. Five patients had an index of 0.35 or less and showed no symptoms of pulmonary insufficiency. The remaining five with a walking dyspneic index between 0.35 and 0.5 had restricted working capacity after operation. Bronchospirometry was performed to determine the relative contribution of each lung to the respiratory effort. Bronchoscopy was performed one week before this investigation to exclude stenosis of the left bronchus and tracheobronchitis. It was found that the isolated function of each lung was quite different from that assessed by clinical examination.

In two patients the contribution of the relatively healthy lung was insufficient, markedly interfering with pulmonary function. The loss of pulmonary function was proportional to the extent of the operation. All these tests helped in planning the treatment for pulmonary tuberculosis, since the aim of these investigations was screening of the respiratory status rather than its complete evaluation. Patients with borderline lung function usually have a stormy convalescence. The loss of pulmonary function three months after six-rib thoracoplasty was 25 to 30% and after nine-rib thoracoplasty 40 to 45%. This observation helped in assessing the ventilatory loss that would probably follow operation and was a reason for refusing thoracoplasty in three patients. The probable advantages of thoracoplasty must be calculated on the amount of pulmonary function that would be retained after operation, and the operation should not be undertaken if it is likely to cause respiratory disability.

To improve pulmonary function patients to be subjected to thoracoplasty were taught to increase their breathing reserve by localized breathing exercises, especially diaphragmatic breathing, and breathing through the lower part of the chest while simultaneously relaxing the upper part. This also helped in preventing postoperative complications. Physiotherapy and exercises of the shoulder and

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The items in these letters are contributed by regular correspondents in the various foreign countries.

back muscles were used to prevent scoliosis and deformity of the shoulder. These helped in preserving pulmonary function and working capacity.

Psoas Abscess.—Risko and Varga (*Indian Journal of Surgery*, vol. 21, February, 1959) stated that the findings on palpation in patients with psoas abscess are not always reliable. They tried to correlate radiologic changes with findings at operation in 30 such patients. Changes in psoas muscles such as enlargement of this muscle or disappearance in its contours occur in other conditions besides tuberculous spondylitis such as abscess of the muscle itself, hematoma, perforation of a paranephric or appendicular abscess, rarely primary tumors, and sometimes after major abdominal or renal operations. Roentgenologic examination reveals only the suprapelvic part of the psoas contour while the lower part if affected can be detected by palpation. In obese patients with intestinal flatulence the use of tomograms has given good results. Of the 30 patients studied retroperitoneal exploration was performed on both sides in 5 and on one side in 25, revealing 40 to 500 cc. of pus or calcified caseous debris. Palpatory findings were negative in 11, all of whom were found to have psoas abscess at operation, 7 unilaterally and 4 bilaterally. Many of them had calcified abscesses the size of a hen's egg or smaller in the region of L-1 to L-3. Six had radiologic evidence of psoas abscess before operation on both sides, and 18 had it on one side. The radiogram was negative in four and doubtful in two because of gas formation.

Since all these at operation were found to have psoas abscess, even the roentgenogram is not always a reliable criterion, although in most of the patients the presence of an abscess in the psoas muscle was assumed on the basis of muscle enlargement or disappearance of the muscle border. Six patients had calcified debris filling the abscess cavity. All but one were children aged 4 to 11; the exception was an adult aged 31 in whom symptoms had started at the age of 14 years. The presence of calcified debris as evidenced by the roentgenogram indicated an early onset of the disease process in childhood. These lesions are not quiescent, as is usually believed. In three of six patients with calcified debris tubercle bacilli could be demonstrated, and five patients were proved to have active tuberculosis by histological examination. Thus the mere presence of calcification does not assure an entirely quiescent lesion. Of the remaining 24 patients culture was positive in 19 and there was histological evidence of tuberculosis in 23. Postoperative roentgenograms were taken in 15 who had preoperative radiologic evidence of psoas abscess. The psoas shadow became normal in 11 and was unchanged in 4, the cause of the persistent change in contour being an organizing hematoma or cicatrix as no pus was obtained on aspiration.

Intervertebral Disk Protrusions.—Ramamurthi and Jaganathan (*Indian Journal of Surgery*, vol. 21, February, 1959) reported a series of 47 patients with sciatica who were operated on. Of these 36 had single lateral protrusions of intervertebral disks, 4 had multiple disk protrusions, and 7 had central disk protrusions. A hemilaminectomy or quadrilaminectomy was performed on patients who had lateral disk protrusions with the patient lying prone with the pelvis and chest well supported. The dura on exposure when palpated felt hard if there was a disk protrusion. The nerve root was displaced medially to expose the protrusion.

Of the patients with lateral disk protrusions 70% had them between the dura and nerve root. The site of rupture could be seen in the annulus fibrosus which was incised when the nucleus pulposus protruded and could be easily picked up. The results were good when the disk came out as a full sequestrum. If it required the punch and scoop to get the nucleus out, postoperative pain in the back often persisted. Postoperative results were good when the patients were carefully selected for operation. In those with compression of the cauda equina a complete laminectomy was preferred. Results for central disk protrusions were good and recovery was complete. Those who had lumbar disk protrusions with predominantly orthopedic signs and without objective neurological signs did well with rest in bed and traction on both legs. If symptoms persisted in spite of such treatment, operation was indicated and fusion of the spine after removal of the disk might be considered.

Anesthesia in Thoracoplasty.—Singh and Kamra (*Indian Journal of Tuberculosis*, vol. 6, March, 1959) reported a series of 400 patients who had thoracoplasties. In 47 of these spinal anesthesia was induced with a 1:1,500 solution of dibucaine, with the patient lying on the sound side. The disadvantages of this method of anesthesia were the profound drop in blood pressure and the fact that coughing is not effective and is accompanied by some paradoxical movement. Regional anesthesia, alone or in combination, was used for 348 patients; thiopental, nitrous oxide, oxygen, and ether for 3; and ether endotracheally for 2. Of the 348 patients only 29 required supplementary anesthesia, either with thiopental or ether, regional anesthesia alone being used for 319. The advantages of this anesthesia were that full cooperation of the patient was possible; respiratory movements were minimal; paradoxical respiration was minimal; the use of diathermy was possible; bleeding was less; and dissemination of the underlying tuberculosis was minimal. Respiration was not hampered by the semiprone position, the condition of the patient at the end of the operation was much more satisfactory, and postoperative nursing care was easier as the patient was fully conscious and cooperative.

All patients between 10 and 15 years of age were operated on under regional anesthesia alone. None of the patients had any other tuberculous lesion. They were usually operated on in the lateral or semiprone position. Procaine was the preferred drug for regional anesthesia, a 0.5% solution for wheal raising and infiltration and a 2% solution for nerve block. The usual time taken for administering anesthesia was 20 to 30 minutes, and the effect lasted for about 3½ hours. Ten patients were given thiopental in addition to regional anesthesia, and 19 were given ether. Blood transfusion was not required in most of the patients operated on under this anesthesia. Paradoxical respiration was not common. A tear in the pleura occurred in 37 patients, but this was well compensated for in those in whom the vital capacity was good. There were four deaths in the series, all due to paradoxical respiration. Postoperative retention of urine developed in some patients on whom spinal anesthesia was used. Paralytic ileus occurred in one patient after operation, spasm of the vessels of the arm in one, and wrist drop in two.

Cor Pulmonale and Tuberculosis.—S. C. Kapoor (*Indian Journal of Tuberculosis,* vol. 6, March, 1959) stated that cor pulmonale has been diagnosed more and more frequently in recent years as a complication of pulmonary tuberculosis. The diagnosis is based on the absence of any other heart disease, the presence of definite heart failure or at least two of the common clinical features, and/or unequivocal electrocardiographic evidence. Most of the cases reported here were discovered during the last 18 months. In the authors' series of 66 such patients the youngest was 6 and the oldest 66 years of age. The known duration of the pulmonary disease before the diagnosis of cor pulmonale varied between six months and 28 years. Twenty-one patients had no cardiac symptoms but 10 of these had suggestive clinical signs. The most constant physical sign of cor pulmonale was a loud pulmonary second sound which was present in 50 patients. Parasternal heaving, although not well developed in all, was present in 33.

Roentgenograms were not of much diagnostic help. The best diagnostic help was the ECG. Thus right ventricular hypertrophy of various grades was present in 39, negative T waves in two leads or more in 26, right bundle–branch block in 11, and extraordinarily high symmetrical T waves in 5. Of the 66 patients 18 died. Although cor pulmonale does occur as a complication of pulmonary tuberculosis, its diagnosis is not always easy. Accentuation of the pulmonic second sound was the principal finding and even this may be absent. In half of the cases the diagnosis could not have been made clinically and an ECG was required. The importance of diagnosing this condition lies in the fact that the cardiac involvement can be checked if detected early enough. Control of secondary lung infection is important in these patients and this alone may help in their treatment.

ISRAEL

Vital Statistics.—The infant death rate dropped to 30.9 per 1,000 in 1958 as compared to 33.6 in 1957. The general death rate was down to 5.62 per 1,000 from 6.18 in 1957. An increase in hospital capacity from 3.03 beds per 1,000 population last April to 3.1 is expected in 1959.

***In Vivo* Staining in Bone Tumors.**—S. Schorr and co-workers, at a meeting of the I. M. A. in Jerusalem, stated that alizarin red S given intravenously by drip infusion to patients having malignant bone tumors had a definite affinity for new bone formation in and around malignant foci. At autopsy the bones gave evidence that malignant foci stained with alizarin were well delimited and even minute foci were easily visible. Both predominantly destructive and predominantly productive malignant metastases had an affinity for alizarin red S. The microscopic appearance of the stained foci showed that even the so-called osteolytic type of bone metastases had active new bone formation. Iodinated alizarin compounds are being prepared to be used as possible x-ray contrast mediums.

Intervertebral Disk Syndrome.—D. Michaeli and co-workers (*Harefuah* 45:265, 1958) treated 24 patients who had intervertebral disk syndrome with ACTH and chlorpromazine in order to reduce the edema of the traumatized nucleus pulposus and the accompanying muscle spasm. Active exercise was encouraged in these patients. The optimum effect was achieved with intravenous infusions of 10 to 20 mg. of ACTH and 50 mg. of chlorpromazine in 500 ml. of normal saline solution over a period of eight hours. The number of infusions usually varied from 1 to 5, although some patients required more. Several patients received corticosteroids after the course of infusions. In most patients dramatic relief from pain occurred within a few days after starting treatment, often within 24 hours, and in most there was an objective improvement with disappearance of difficulty in straight-leg raising and reappearance of the ankle jerks. In nine patients, however, objective improvement was not remarkable, despite rapid subjective improvement. In three there was no improvement, and diskectomy was performed. These three patients had the most severe lesions from the clinical point of view. In addition to the usual findings sensory disturbances and loss of the ankle jerks were present. Only 2 of the 15 patients in whom the previous attack had lasted less than three months failed to improve. When the previous attacks had lasted longer, the treatment was less effective.

NORWAY

Anticoagulant Therapy.—As Professor Owren pointed out, the Quick method for the control of anticoagulant therapy is not accurate enough and his own method is technically difficult, requiring the services of a specially equipped laboratory (*Tidsskrift for den norske laegeforening*, April 1, 1959). He has devised a new method. The all-in-one reagent he uses is dehydrated and vacuum-sealed. It contains an active cephalin-lecithin preparation, a weak thromboplastin reagent, both in optimal concentrations, stabilized bovine plasma completely free of the four factors to be determined, and calcium in optimal concentration. The reagent keeps for at least a year and tests have shown unchanged activity after 30 days' storage at 47 C. In solution and ready for use the reagent's activity remains constant for at least 12 hours at room temperature and 72 hours at 6 C. The new method has been worked out for capillary blood, citrated venous blood, and citrated plasma. Only 0.1 ml. of blood is needed. The test is quickly made and the results are known in two or three minutes. The new method eliminates the faults of earlier methods and reduces the risks of hemorrhages to a minimum. Its simplicity means that a minimum of experience is required of physicians who wish to make use of it.

Open-Door Policy in Asylums.—On the women's side of the Gaustad state asylum for care of the insane near Oslo much has been done in recent years to dispense with the locked-door policy, in spite of the difficulties experienced in retrieving escapees. The shops in the neighborhood have learned to deal helpfully with them, and their brief outings teach them to adjust themselves better to their circumstances within the hospital. Due in part to advances in pharmacology, vocational therapy, and greater freedom in the asylum, the past seven or eight years have shown a marked increase in the hospital's annual turnover. According to P. Sundby and co-workers (*Tidsskrift for den norske laegeforening*, April 1, 1959) the number of new admissions rose from 107 in 1950 to 189 in 1957, and the number of discharges from 96 to 173 in the same period. The number of readmissions remained at 45 to 50%. Since the asylum's capacity has been increased by the increase in turnover the waiting list has been so shortened that it is now rare for a new admission to be much delayed.

How a General Practitioner Spends His Time.—Working as a general practitioner in a farming and mining community Dr. O. H. Iversen (*Tidsskrift for den norske laegeforening*, April 15, 1959) kept a minute record for 18 months of all he did. The treatment of respiratory diseases accounted for 15% of his practice. Mental and emotional diseases accounted for only 3%. Among the laboratory tests performed hemoglobin determinations came first with 688, sedimentation rate determinations came second with 390, and microscopic examinations of urinary sediment came third with 94. Among the operations performed dental extractions numbered 653, incisions 80, punctures 14, and sutures of wounds 19. In 56 patients the tympanum was punctured, and in 28 warts or small tumors were removed. In 30 patients varicose veins were treated by injection. Each consultation took an average of 23 and each house call 54 minutes. The relatively high income of many physicians in private medical practice is only possible because of the long hours they put in.

Training Medical Students Abroad.—After World War II many prospective medical students had to go abroad because there was no room for them in Norwegian medical schools. By the end of 1958 the number of these medical expatriates was 690. Commenting on their fate in *Tidsskrift for den norske laegeforening*, April 15, Prof. A. Ström pointed out that they outnumbered the home-trained medical students, since the present entry of students to Norway's two medical schools is only 130 yearly. Before 1958 it was only 100 yearly. At present there are hospital vacancies enough for both home-trained and foreign-trained students, but the author foresaw a not distant day when the physician returning to Norway will find the medical profession painfully overcrowded. While he would not discourage the prospective physician with a natural bent for the art of healing he suggested that when earning a living is the main objective, the medical student contemplating a costly course of studies abroad would do well to think twice.

SWEDEN

Medullary Sponge Kidney.—Medullary sponge kidney is a condition in which all or part of the medulla of the kidney presents a sponge-like appearance, owing to the presence of multiple cysts and cavities formed by dilatation of the collecting tubules. N. Lindvall (*Acta radiol.* 51:193-206 [March] 1959) reported on a series of 35 patients with this condition. According to the roentgenograms the changes were bilateral in 23 and unilateral in 12. The ages of the patients ranged from 16 to 62 years. The progress of some patients was followed for as long as 16 years. In all the diagnoses were made from the urograms. The changes were of all grades, from a few cavities in a single pyramid of one kidney to multiple cavities in all the pyramids bilaterally. Enlargement of the involved pyramids was observed in 31 kidneys. Even in parts of the kidney where no cavities were visible some kidneys showed enlarged papillae and general hypertrophy, suggestive of the presence of changes which had not been directly shown, and the calices of the enlarged papillae were also enlarged.

In all but two patients from one to several hundred calculi were present, most of them round and dense and sometimes disposed in groups, thus presenting so distinctive a picture that the diagnosis was suggested even in conventional roentgenograms. If at the same time there was enlargement of the kidney, the diagnosis could in some cases be made without recourse to urography. During the observation period the only roentgenologic changes were signs of pyelonephritis, the formation or disappearance of stones (after passing), or the appearance of hydronephrosis due to the passage of a calculus. Malformations within the urinary tract, such as caliceal cysts and hypoplasia, were found in only four patients.

The conditions and changes that might be roentgenologically confused with medullary sponge kidney are renal tuberculosis, papillary necrosis, caliceal diverticula and cysts, tubular stasis, and various forms of nephrocalcinosis. As the clinical findings of medullary sponge kidney are determined solely by the complications, the diagnosis rests with the roentgenologist; it is facilitated by the fact that the changes do not appreciably affect the excretion of contrast medium. Medullary sponge kidney is so common that it deserves more attention than it has received.

Mortality and Muscle Relaxants.—The use of muscle relaxants is steadily increasing. T. Gordh (*Acta anaesth. scandinav.* 3:35-40, 1959) studied the use of such drugs in patients undergoing urologic, abdominal, and cancer operations. After intravenous injection of the drug the patients breathed 100% oxygen. Intubation if indicated was performed under the relaxation obtained with succinylcholine chloride, the dose usually not exceeding 50 mg. The required depth of anesthesia and relaxation were maintained by injections of a 5% narcobarbital solution and succinylcholine, administered at appropriate intervals. The gases inhaled consisted of a mixture of oxygen, 1 liter per minute, and a maximum of 3 liters of nitrous oxide per minute in a semiclosed system. In intra-abdominal surgery local infiltration of 0.5% lidocaine with epinephrine was occasionally used along the line of incision. In the years 1946 to 1957, in a total number each year of 4,000 to 5,000 patients, the postoperative mortality varied yearly from 1.1 to 1.6% while muscle relaxants were used with a frequency increasing from 1.0% in 1947 to 36.7% in 1957. The increase in the use of muscle relaxants occurred at the expense of the use of ether and spinal and local anesthetics. From 1944 to 1945 no muscle relaxants were used for operations on the biliary system. Succinylcholine was introduced in 1950. While the use of muscle relaxants in biliary operations has increased from 0 to 95.3%, the mortality has not changed.

Circulatory Disturbances in Osteoarthritis.—A. Hulth (*Acta orthop. scandinav.* 28:81-89, 1958) reported that intraosseous venographies of femoral heads were performed on 15 patients with osteoarthritis. Normally venograms showed circumflex veins. In patients with osteoarthritis of the hip venograms were characterized by accumulation of dye in the femoral head, evacuation of the contrast medium from the head occurring mainly via medullary veins coursing distally into the femoral shaft. The injection in patients with osteoarthritis was painful, but in persons with normal or slightly affected hips it was almost painless. In patients with osteoarthritis the venous pathways from the site of injection were entirely changed. The contrast medium in the diseased hips had to traverse a much longer intraosseous course before entering the large extraosseous veins, i. e., the femoroiliac veins. The pathological cancellous tissue in an arthritic femoral head created conditions for intraosseous venography that were entirely different from those encountered in normal bone. The contrast medium in the former might take a "false" course. It looked, however, on the roentgenogram as if the injected contrast medium had spread out in the entire femoral head and could therefore run out via epiphysial and metaphysial veins, if such veins existed. It was thus possible that these so-called retinacular veins had ceased to function in the severely osteoarthritic hip. The venogram might indicate a real venous stasis.

Diskography.—S. Nordlander and co-workers (*Acta orthop. scandinav.* 28:90-102, 1958) made a roentgenologic analysis of 73 patients with low back pain, sciatica, or both. Operation had been performed on all and most had undergone both myelography and diskography. The authors were unable to show that diskography was superior to myelography for routine diagnosis of herniation of an intervertebral disk, but it was difficult in part of this series to make a diskographic analysis. The authors concluded that there was good reason to stick to the use of myelography with injection of water-soluble contrast medium in routine examination for disk herniation producing nerve-root compression in patients with low back pain and sciatica, but that diskography could be used as a complementary method of examination.

Epiphysiolysis Capitis Femoris.—N. Lindström (*Acta orthop. scandinav.* 28:131-146, 1958) reported that between 1944 and 1955 54 hips in 51 patients were treated at the orthopedic clinic in Härnösand for epiphysiolysis of the femoral head; 26 hips were fixed in situ, 4 were treated by closed reduction, and subcapital wedge osteotomy was performed on 24. In one of the latter no internal fixation was performed, but all the others were fixed with a three-flanged nail except one which was fixed in situ by a wing screw. The follow-up period was about 4½ years. There was no necrosis of the femoral head in those hips nailed in situ. One patient treated by closed reduction had such a necrosis. Of those who underwent subcapital wedge osteotomy one had total and one partial necrosis of the femoral head, and one had traumatic arthritis with destruction of the joint cartilage. There were no poor results from fixation with a three-flanged nail, so this method of fixation was recommended by the author. Because the danger of necrosis occurring in patients with extensive slipping is great, the reduction must be handled with extreme care. The results of the subcapital wedge osteotomies with simultaneous nailing were satisfactory.

Depressions in Patients Treated with Reserpine.—K. Jensen (*Acta psychiat. et neurol. scandinav.* 34:195-204, 1959) reported on 11 women, all hospitalized because of depressions appearing after 1 to 10 months' treatment with reserpine for hypertension in daily doses of 0.50 to 0.75 mg. One patient had been given a whole-root preparation of Rauwolfia serpentina, containing 0.3 mg. of reserpine. The patients were aged from 42 to 76 years. A predisposition to depression was present in five. The symptoms were a deep sensation of unhappiness, frequent crying, restlessness, and anxiety. One patient attempted suicide. Seven patients were given electroconvulsive treatment, two a combination of electroconvulsive treatment and chlorpromazine, and two had chlorpromazine only. The treatment gave good results in all. About six months after leaving hospital two patients were again given reserpine and had to be readmitted to the hospital because of depression. Since the discontinuation of treatment with reserpine did not always bring about cessation of the symptoms, it was not supposed that reserpine was the only cause of symptoms but rather that it was a precipitating factor.

Multiple Injuries.—I. Palmer (*Opuscula med.* 4:83-90 [March] 1959) studied a series of 65 patients with multiple injuries. These patients had an average of 33 injuries each. Manifest shock was present in 41. The treatment should be directed against the following conditions in the following order of priority: (1) shock, continuous bleeding, respiratory obstacles, and epidural hematoma; (2) intestinal and gastric injuries; (3) large wounds; (4) fractures; and (5) head injuries. On account of the multiplicity of the injuries treatment of fractures must be divided into a primary and a secondary definitive phase. The healing of each injury seemed not to be delayed by the presence of other injuries.

Prognosis of Cardiac Infarction.—Helander and Levander (*Acta med. scandinav.* 163:289-304, 1959) studied some of the factors in the composition of the material which could influence the primary mortality and the long-term prognosis of patients with cardiac infarction. A series of 286 patients were divided with regard to the age, sex, and severity of the first attack of the myocardial infarction. The primary mortality was 32%. The difference in the primary mortality in relation to the age and sex of the patients was most clearly marked between the older and the younger women, being 48 and 6% respectively. While it was postulated previously that women had a higher mortality than men, this seemed to apply to the older women only. The difference between the older and the younger groups was less marked among men. Differences in the composition of various materials regarding the age and sex of the patients could therefore decisively influence the result.

In estimating the 5-year survival rate the authors analyzed the 232 patients who survived their first attack of cardiac infarction. After five years 58% were still alive. The severity of the infarction did not influence the continued course as markedly as the primary mortality. The difference which became apparent in the primary mortality between the younger and the older women was not matched by a similar difference in five-year survival rate, 62 and 49% respectively. A comparison between the five-year survival rate after the first attack of myocardial infarction in this series, on the one hand, and in a Stockholm population of the same age, on the other hand, showed a greatly increased mortality among the former. Autopsy showed that in 42 of the 80 patients examined there was thrombosis in the coronary artery. There was a coronary embolism in one.

There proved to be a good correlation between the electrocardiographic and the autopsy findings, as regards the localization of the infarction. Among the electrocardiographic changes the atrioventricular and the intraventricular heart block seemed to signify an essentially aggravated prognosis, with a 69% primary mortality as against 23% in patients whose ECG showed no such changes. A complete regression of electrocardiographic changes was noted in 23 paients. Of the 135 who survived for five years 85 were still alive at the follow-up examination time, i. e., on the average eight and one-half years after the myocardial infarction. Of the latter 78 were given a control examination; 21 were normally active and 23 were completely disabled. Twenty-four were free of angina pectoris. Of the abovementioned 78 patients 23 had had at least one relapse.

Primary Hyperparathyroidism.—J. Hellström (*Nord. med.* 61:551-556 [April 9] 1959) studied a series of 115 patients with hyperparathyroidism observed during the period 1930-1957. In more than 80% the diagnosis was made after 1950. Radiologically observable changes in the kidneys in the form of calculi or nephrocalcinosis were noted in 85%. In 52 patients 103 operations for renal calculi were performed. One patient underwent six operations. The author believed 3 to 5% of all cases of renal calculi were due to hyperparathyroidism. In all patients with hyperparathyroidism, even those in whom no radiologic changes in the kidneys were seen, a renal lesion was present. In the earlier stages this was functional and transient after successful parathyroidectomy; in the later stages it became structural, persistent, or progressive although the hyperparathyroidism was cured by operation.

As a manifestation of this renal lesion there was always impairment of the concentrating power of the kidney. Normal concentrating power almost surely excluded hyperparathyroidism. Among these patients 70% had hypertension and in several this led to incapacity or death from cerebral complications. The main cause of the hypertension was probably the renal damage. As regarded the skeletal changes osteitis fibrosa occurred less often in recent than in former times. In 8 patients the first symptom was a giant-cell tumor in the upper or lower jaw. The skeletal changes always healed, functionally if not anatomically. Peptic ulcer occurred in 33% of the males and 5% of the females. The diagnosis of hyperparathyroidism rested on clinical symptoms, radiologic examination, and laboratory procedures. Even a slight rise in the blood calcium level (10.5 to 11.0 mg. per 100 ml.) should arouse suspicion of hyperparathyroidism.

The prognosis of untreated hyperparathyroidism was generally poor. The prognosis after parathyroidectomy depended mainly on the degree of renal damage at the time of operation. In 22% of the author's series the operation was unsuccessful or incomplete. The reasons for this were removal of an insufficient number of glands in multiple adenoma or primary hyperplasia; confusion with lymph nodes or adenoma of the thyroid; very small adenomas; and abnormal location, the adenomas being enclosed in the thymus or the thyroid, or displaced to the mediastinum. In view of these difficulties and of the many yet unanswered questions concerning the pathogenesis of hyperparathyroidism, patients with this disease should be referred to hospitals that have the best facilities for its treatment.

New Operation for Gastric Ulcer.—Instead of reducing the volume of the stomach by half or more in the course of a partial gastrectomy, an operation that causes lasting inconvenience to about 50% of all patients so treated, Dr. S. Hedenstedt of Luleå uses 4 to 6 in. of small intestinal tissue to replace the resected stomach and retain the stomach volume. The follow-up period in about 33 of his series of about 100 patients treated by this method was two years, and in these patients the operations proved very successful. Another advantage of the method was that it offset the postoperative effect of reduced formation of blood corpuscles, formerly a frequent result of gastric operations. The 3 or 4% of patients who suffered from disabling complications after the first operation have had a second operation with surprisingly good results.

Professor Crafoord Honored.—Prof. Clarence Crafoord of Stockholm, the well-known thoracic surgeon, was named Doctor Honoris Causa at the University of Córdoba in Argentina. Last year Professor Crafoord and his co-workers performed a series of operations in Argentina and demonstrated their heart-lung machine.

Implantation Metastases in Renal Pelvis.—A. E. Nilson (*Acta chir. scandinav.* 116:306-314, 1958/1959) reported on five patients who had recurrent tumors of the bladder with secondary tumors of the renal pelvis. In three a urethral catheter was introduced and retrograde pyelography performed on the involved side to verify the diagnosis of pelvic tumor. Excretion in the affected kidney had ceased in one of these patients and was lowered in the others. In no instance had ureteral catheterization preceded the discovery of the renal pelvic tumor. Vesicoureteral reflux was detected prior to or at the same time as the renal pelvic tumor, three to eight years after the treatment of the initial bladder tumor. In no case in which the orifices were judged to be normal on cystoscopic inspection could vesicoureteral reflux be demonstrated. Cystoscopy revealed appreciable anatomic changes in all the ureteral orifices in which cystography disclosed reflux. There was strong evidence that implantation metastases from the bladder to the upper urinary tract might occur in the presence of defective valvular function with accompanying vesicoureteral reflux, permitting the retrograde transport of tumor cells. When vesicoureteral reflux is demonstrated, frequent urographic examinations of the upper urinary tract should be performed to facilitate early detection of implantation metastases.

Coccygodynia and Rhizotomy.—Bohm and Franksson (*Acta chir. scandinav.* 116:264-267, 1958/1959) reported on 15 patients with coccygodynia, 7 of whom had previously undergone rectal surgery and were treated by division of the lower sacral nerve roots. The operation relieved the pain completely in seven of the eight patients with "idiopathic" coccygodynia and in all seven who had rectal operations. In the patients who had undergone rectal surgery, a neurotraumatic cause of the coccygodynia was an important possibility, according to the authors. One patient was still alive and apparently without metastases. The others died fairly soon after rhizotomy. It is therefore possible that carcinomatous recurrences caused the pain in the coccygeal region. Rhizotomy in these patients must therefore be regarded as a purely denervating operation and as an alternative to chordotomy. The writers commented that the latter operation was a major undertaking and, if done bilaterally, might entail significant disability. A limited root section, the procedure in the present series, involves negligible neurological loss. The drawback of rhizotomy is that spread of the cancer gives rise to pain from other structures. The effect of rhizotomy may thus be transient. The most suitable patients for rhizotomy would seem to be those in whom the pain has long been concentrated in the coccygeal region.

UNITED KINGDOM

College of Surgeons Criticized.—A few weeks ago a Sunday newspaper carried photographs showing the president and council of the Royal College of Surgeons of England listening to the Hunterian oration. The names of the surgeons in the front two rows were given in full under the photograph so that they could easily be identified. In other papers gossip-column writers described a party held in the rooms of the college where stars of a television serial called "Emergency Ward 10" drank cocktails with some of the leading surgeons. All this was part of a publicity drive to get money for new buildings for the college.

This method of obtaining publicity was severely criticized in an editorial by the *British Medical Journal*, which said that if the college wanted money it should obtain it without loss of dignity and without giving publicity to the members of its council. Exception was also taken to full-page advertisements in the *New Statesman* and *Spectator*, announcing a television program called "Surgeon," in which the names of the president and six members of the college council were mentioned, complete with qualifications, distinctions, and honors. Criticism was also made of a picture in a Sunday newspaper of the president of the college rehearsing for a television show. The *British Medical Journal* thinks that bad advice was given to the college by its publicity experts. It would be a pity if the college, in achieving its goal of raising $8,500,000, found that it had lost something more precious than money in the process.

Malignant Melanoma.—Encouraged by successful experience with autogenous marrow replacement after large-field irradiation Westbury and co-workers treated a patient who had disseminated malignant melanoma with a massive intravenous dose of mannomustine hydrochloride, a cytotoxic drug, followed by reinfusion of the patient's own stored marrow (*Lancet* 1:968, 1959). The patient, a woman aged 38, was referred for treatment after the excision of a malignant melanoma over the right scapula. The primary site was irradiated, and after preoperative irradiation an axillary block dissection was performed. Within two months nodules appeared in the scalp, axilla, thorax, and thighs, and, in addition to gross enlargement of the liver, the brain also appeared to be involved. Radiography showed scattered metastases in the lungs. Bone marrow containing 800 million cells was aspirated under anesthesia from the sternum, iliac crests, and vertebral spines and stored at −79 C. Then 3,000 mg. of mannomustine was given intravenously over five days by rapid injection in a continuous 5% dextrose solution drip. In addition the patient received prednisone, perphenazine, tetracycline, and vitamin K. After the course of mannomustine was completed the stored marrow was thawed, reconstituted, and injected intravenously.

Regression of skin nodules began almost immediately, followed by a fall in the lymphocyte concentration and depression of the total leukocyte count. Within a few days headache, vertigo, and vomiting set in. The patient lapsed into unconsciousness and died one week after the marrow reinfusion. Death was due to hemorrhage into a necrotic metastasis in the left cerebellar hemisphere. At autopsy many of the nodules were seen to have regressed and undergone extensive central necrosis.

This case demonstrated that a large dose of a cytotoxic drug may be given with remarkably few side-effects, and yet produce a rapid and dramatic shrinkage of melanomatous deposits. Death from cerebral hemorrhage occurred too soon for the results of marrow transfusion to be seen in the circulating blood, but postmortem examination of the marrow suggested that regeneration was taking place. The rapid and unexpected regression of the deposits was sufficien[illegible] to warrant further trial of this [illegible] advanced cases.

Incidence of Gonorrhea Increasing.—According to a circular sent from the Ministry of Health to local health officers gonorrhea is increasing, particularly among women. In 1951 14,975 new cases in men and 3,089 in women were seen in the venereal disease clinics in England and Wales. In 1957 corresponding figures were 19,695 and 4,737. This represents an increase of 31% for men and 53% for women. This is a real increase and not merely a higher proportion of patients being treated. The increase continued in 1958. The Ministry of Health stated that a relatively small group of promiscuous infected women constitutes the most important factor in the spread of the disease, and it is this steadily increasing group that is the principal cause for concern. Although the number of women known to be infected is much smaller than the number of men, the proportion of the former who remain untreated is probably higher because infection is not so obvious in women. The Ministery of Health has asked local health officers to review arrangements for tracing contacts. This increase in the incidence of gonorrhea may be due to an increase in the number of strains of penicillin-resistant gonococci, to the belief that penicillin has made gonorrhea an easily cured infection, and to the ignorance of the public about the nature of the disease.

Clearance Rate of Insulin.—The rate of clearance of insulin labeled with radioactive iodine from subcutaneous sites in normal subjects and diabetics was studied by Joiner (*Lancet* 1:904, 1959). The labeled insulin was injected subcutaneously into various sites in the arm, leg, and abdomen in 97 control subjects of both sexes, mainly doctors and nurses, and serial counts taken at 30-second intervals over the injection site with a Geiger counter. All observations were made at a constant room temperature of 32 C and a standard injection of 8 units of insulin in 0.2 ml. of physiological saline solution, which corresponds to 1 mc. of radioactivity, was given. As an added protection for the thyroid gland 10 mg. of potassium iodide was given orally to most subjects before the experiment. In men the half-life of the isotope was 67 ± 11 minutes from the arm, 123 ± 18 minutes from the leg, and 76 ± 20 minutes from the abdomen. The corresponding figures for women were 55 ± 7, 99 ± 12, and 76 ± 20 minutes respectively. Variation in volume and concentration of the insulin and in the amount of exercise taken had no significant effect on the rate of clearance. The differences between the clearance rate in the arm and leg and between men and women were statistically significant. The rate of absorption of the insulin was significantly increased by the addition of hyaluronidase.

The radioactive insulin was also given subcutaneously to 41 diabetic patients. The clearance was slower in women than men, and in diabetics whose disease was of long standing than in those whose disease was of recent origin. As in normal subjects exercise had no effect on the rate of insulin clearance, which seemed to increase with age. Delayed absorption was not a significant factor in poorly controlled diabetics. A preliminary study indicated a possible association between lipodystrophy and delayed clearance.

Increase in Incidence of Leprosy.—The Minister of Health stated in Parliament that there are 275 patients with leprosy in the United Kingdom. One member asked why the number of cases has increased from 46 in 1951 to the present figure. He thought that the situation was becoming serious, since the disease is contracted outside the country and brought in by immigrants. In his opinion there should be some regulations to prevent the uncontrolled entry of immigrants suffering from the disease. The minister said that there is no evidence that leprosy is spreading. There are two special units in the country where inpatient treatment can be given. Sufferers from the disease can also be treated as outpatients in the infectious and tropical disease hospitals.

Breast Abscesses and Antibiotics.—According to Knight and Nolan breast abscesses in the puerperium are becoming resistant to treatment with antibiotics (*Brit. M. J.* 1:1224, 1959). They noted that the duration of infection and morbidity in 100 women with puerperal breast abscesses who required hospitalization was greater than in a comparable group studied in the same hospital 16 years ago, before the use of antibiotics. The increase was attributed partly to the widespread use of these. At the moment there is a high degree of antibiotic resistance in the strains of Staphylococcus aureus isolated from puerperal breast abscesses; 93% were found to be resistant to penicillin, 55% to streptomycin, 40% to oxytetracycline, but only 1% to chloramphenicol, which is regarded as the preferred antibiotic. When the organism is antibiotic-resistant the pathological features are modified unfavorably. Tissue necrosis and pus formation are retarded, while repair proceeds uninhibited, but a thick fibrous wall forms around the abscess, delaying resolution and preventing collapse of the cavity after incision. A further result of this increased fibrosis is the tendency to produce unsightly shrunken breasts.

The incidence of mastitis and breast abscess in women delivered in hospital was found to be more than double that in women who had home confinements. This was associated with the heavy colonization of the baby's nasopharynx with organisms from the hospital environment in which it spends the first few days of life. These organisms were the same as those recovered from the breast abscesses, but were different from those carried in the mother's nares. Another important etiological factor in these breast infections was milk engorgement, which often resulted from stopping breast feeding without taking adequate measures to suppress lactation and empty the breasts. At least 33% of those with breast abscesses had stopped breast feeding as soon as they left hospital. The authors suggested that the incidence of puerperal breast abscess could be reduced by allowing mothers who wish to bottle-feed their babies to do so straight away. Lactation can be suppressed with diethylstilbestrol in these patients and in those in whom breast feeding is stopped for any reason. Antibiotics should be given if infection is suspected, but if there is no local response to these after two days their administration should be stopped. The antibiotic least likely to cause resistance is chloramphenicol.

Mass Radiography and Cancer of Lung.—It is generally accepted that mass radiography of the chest offers the best known single means of detecting, as rapidly and as economically as possible, significant intrathoracic lesions in the general population. National morbidity figures suggest that at present mass radiography does not find more than 10% of all new cases of cancer of the lung in England and Wales, but it can be an effective method for locating early cases before symptoms appear. Posner and co-workers attempted to assess the value of conventional routine mass radiography in detecting early asymptomatic cases of carcinoma of the lung by comparing cases found by this means with those discovered among patients referred by general practitioners because of suspicious symptoms (*Brit. M. J.* 1:1213, 1959). A comparison of the resectability of the lesions in the two groups of patients was made. A slightly higher rate of resectability was found in those discovered in routine mass radiography surveys, although this was not statistically significant. The two-year survival rates, irrespective of treatment, were higher in the mass radiography group (25%) than in the general practitioner referrals (20%). A larger proportion in the mass radiography group underwent lobectomy than in the other group. The patients with symptoms were usually referred by general practitioners without undue delay, and most resections were performed within the first two months after radiography.

The most disturbing finding was the small number of silent lesions that were discovered by routine mass radiography. This might have been due to radiographic technique, because small peripheral lesions were often not distinct enough to be noted, even by experienced observers, on 35-mm. film. At present both cancer of the lung and active tuberculosis are found predominantly in men over 35, and it is in this age group that the main effort of mass radiography should be concentrated. It is recommended that more 100-mm. x-ray units, with their superior quality and size of film, should be installed to deal with the larger number of patients, particularly men in the critical age group.

Xanthocillin.—The local use of a new antibiotic, xanthocillin, was described by F. R. Bettley (*Brit. M. J.* 1:1226, 1959). Xanthocillin, derived from Penicillium notatum, was isolated in the form of yellow crystals containing two distinct chemical components with similar properties. It is not suitable for systemic use because of its toxic properties and poor absorption, and so it is limited to topical application. In vitro tests have shown that most of the common gram-positive and gram-negative pathogens, including Proteus and Pseudomonas aeruginosa, are sensitive to the antibiotic, which also has some suppressive action on Mycobacterium tuberculosis and some pathogenic fungi and yeasts. Bacterial resistance develops very slowly, and no cross-resistance to other antibiotics has been reported. Patch tests showed no irritating or sensitizing properties. Bettley has treated infected eczematous and intertriginous eruptions with a cream containing xanthocillin. Most of the patients had already been treated with other antibiotics or with antiseptic applications. In no case did the antibiotic act as a primary irritant or sensitizer. In some patients there was a rapid and striking improvement, after other antibiotics had failed, while in others it was of no apparent benefit. The general impression was that the results were favorable, and that a more extensive trial was warranted.

Carcinogenesis and Cosmetics.—In a debate in the House of Lords a member asked if azo or other synthetic dyes were used in lipsticks, whether such dyes were toxic or carcinogenic, and whether any control was exercised over their incorporation into lipsticks. Dyes are in fact used in lipsticks, and they may be absorbed by ingestion or through the skin. There is no control over their use, as there is in the manufacture of foodstuffs. Thirty synthetic colors are allowed as additives to food, but none are known or suspected carcinogens.. Nearly 200 dyes and pigments are used in the cosmetics industry, excluding those used in hair dyes. It is suggested that only certain dyes should be used in the manufacture of cosmetics. This would reduce any carcinogenic hazard. Apart from dyes estrogens are sometimes added. These are known to cause cancer in animals and probably in man. Unlike substances having a direct toxic action the estrogens are only carcinogenic when used for 20 years or more. Other toxic results such as dermatitis make their appearance within a short time. There is much to be said for controlling the constituents of cosmetics and insuring that no known or suspected carcinogenic agents are used in their manufacture.

Too Little Spent on Medical Research.—At the annual meeting of the Royal Society of Health, Lord Cohen of Birkenhead, its president, said that Britain is spending far too little on medical research. Although much has been accomplished in the conquest of disease, four scourges call for intensive research. These are cancer, heart disease, arthritis, and mental illness. Cancer is responsible for about 20% of all deaths in Great Britain. Coronary disease, strokes, high blood pressure, and other forms of heart disease have accounted for 50%. Many of the most killing forms of heart disease occur among active persons in their 40's and

50's. Rheumatism, while not a fatal disease, is a major cause of disability. It is disconcerting to reflect that half of the total hospital beds in the country are occupied by patients suffering from mental illness. Thus 1 in 250 of the population now occupies a bed in a mental hospital. Research requires not only new ideas but also money. Intelligent expenditures for research are limited by the number of men and women of sufficient quality and dedication who can be found to do this work, but even so, said Lord Cohen, we could and should spend far more than we do.

Working Women.—At the same meeting Dr. Alice M. Stewart said that modern society was ill-adapted to the needs of women over 40 years of age. She opposed the notion that woman's place is in the home and added that one could as well say, "Man's place is behind a wheelbarrow." On the other hand the most contented mothers and wives are the ones who have succeeded in combining housework with other occupations. More day nurseries are needed so that young mothers can go out to work. Some of them could run the nurseries.

Drug Output Doubled.—Britain's drug industry is expanding. Output and exports have more than doubled since 1948, yet the increase in labor has been less than 10%, according to the annual report of the Association of the British Pharmaceutical Industry. Sales to the National Health Service (NHS) accounted for only about 33% of the industry's output. Australia was the chief overseas buyer, followed by Nigeria, New Zealand, and the Union of South Africa. Throughout the past 10 years the cost of drugs has loomed large in Parliamentary and public discussions of the NHS, although manufacturers and wholesalers still receive no more than 7% of the total NHS expenditure. There is a need to assemble facts about the provision and use of drugs, particularly the savings to the NHS and the economy at large which the use of modern drugs produce, so that the question of NHS expenditure on drugs can be viewed in its true perspective. Members of the association informed the committee of the British association that they would welcome the adoption of the metric system in Great Britain and could implement it within a year. Most members also favored a decimal monetary system.

Mental Health.—Mr. Walker-Smith, Minister of Health, called on county and borough councils to expand their mental health services to meet the new concept of care of the mentally disordered in the community, as far as possible, rather than in hospital. The new order will require close cooperation among the hospital, local health officers, and family doctors. When more of the mentally disordered are being helped to live independent and useful lives in the community, more will remain under the care of family doctors. In the treatment of mental patients three principles that are sometimes in conflict must be balanced: the patient's treatment, the patient's liberty, and protection of the community. Local health authorities are urged to provide training centers for mentally disturbed children up to the age of 16 years, who are regarded as suitable for training. These children should live at the center from Monday to Friday, or for a school term, returning home at week-ends or during holidays. There should be regular medical inspection, dental treatment, meals, and milk provided on lines similar to those in schools for normal children. Adult training centers are also needed but should be given a lower priority.

Luminous Watch Dials.—At the same meeting Sir Ernest R. Carling said that a Swiss firm was using radioactive strontium to luminize watch dials. This is known to have done serious harm to one wearer. These watches may be bought in Great Britain.

Tetanus from Wound Dressings.—After the occurrence of five postoperative cases of tetanus within a fortnight in one hospital the Medical Research Council requested the Public Health Laboratory Service to investigate possible methods by which infection with tetanus spores might be conveyed in hospitals. The study was made by 14 laboratories. All the materials commonly used for wound dressings were examined by boiling samples with nutrient broth. This kills all organisms except tetanus spores. Growths surviving this procedure were then subcultured on slopes of horse blood agar and confirmatory tests of identity of Clostridium tetani were made. Cl. tetani was found in samples of absorbent cotton, gauze swabs, and stockinet. The most frequently contaminated form of dressing was unbleached absorbent cotton; 100 samples of this were examined in various parts of Great Britain and tetanus spores were found in 20.

On the other hand only one packet in 122 of bleached absorbent cotton was found to contain the spores. The use of unbleached cotton would explain outbreaks of tetanus infection in hospitals where in other respects every attempt is made to preserve sterility. It is therefore recommended that all dressings and particularly absorbent cotton be sterilized before being taken into the operating rooms. Other possible sources of infection were investigated. Tetanus spores were found in the air intake ducts and in the wall plaster of operating rooms. Rubber gloves were not examined, but it is well known that they may be dusted with potentially contaminated powder and are by no means always properly sterilized. It was concluded that every attempt should be made to prevent tetanus spores being carried into the operating room by air, street dust, dressings, or any other route.

CORRESPONDENCE

OXYGEN IN THE THERAPY OF CYANIDE POISONING

To the Editor:—During experiments on sublethal intoxication of rats by intravenously given potassium cyanide (Levine and Wenk, *J. Nerv. & Ment. Dis.*, to be published), slightly more cyanide was required to induce brain lesions if oxygen was administered than if the experiment was conducted in air. Further work on mice showed that the LD_{50} of potassium cyanide was slightly increased (10 to 20%) by administration of oxygen; survival time after fatal doses was increased also. These results suggested the possibility that oxygen might be useful in the therapy of cyanide poisoning.

Textbooks on pharmacology and toxicology advise the nitrite and thiosulfate method of Chen and Rose (J. A. M. A. 149:113, 1952; 162:1154, 1956) as the treatment of choice. In most textbooks oxygen is not mentioned or is advised only when respiration has ceased and artificial respiration is required. Salter (Textbook of Pharmacology: Principles and Application of Pharmacology to the Practice of Medicine, Philadelphia, W. B. Saunders Company, 1952) stated that the rationale for the use of oxygen was not very sound because cyanide produces a histotoxic anoxia in which tissues are incapable of utilizing oxygen. Locket (Clinical Toxicology: Clinical Diagnosis and Treatment of Poisoning, St. Louis, C. V. Mosby Company, 1957) went further and stated: "If a cyanide has been taken do not waste time with . . . artificial respiration or administration of oxygen." However, Sollmann (Manual of Pharmacology and Its Applications to Therapeutics and Toxicology, ed. 8, Philadelphia, W. B. Saunders Company, 1957), referred to the work of Gordh and Norberg (*Acta physiol. scandinav.* 13:26, 1947) who found that rabbits in a preterminal state of poisoning after receiving lethal doses of cyanide could be saved by oxygen.

Ferraro and Kilman (*Psychiatric. Quart.* 7:115, 1933) and Jervis (*Riv. pat. nerv.* 50:410, 1937) stated that cyanide poisoned cats were revived by oxygen. Ferraloro (*Sperimentale* 84:115, 1930) reported that survival of cyanide-poisoned guinea pigs was prolonged by increased oxygen tension. Wirth (*Zentrabl. f. Gewerbehyg.* 24:258, 1937) found that oxygen speeded the recovery of cyanide-poisoned cats and rabbits, and carbon dioxide was not indicated. Paulet (*Arch. internat. physiol.* 63:340, 1955) found that oxygen saved dogs that had received lethal doses of cyanide, and its effect was even greater when given under slightly increased pressure. H. J. Taylor (personal communication) was able to save cyanide-poisoned cats by inducing a high-pressure oxygen convulsion!

Breathing pure oxygen increases the arterial saturation of hemoglobin above the normal 97.5% level and increases the amount of oxygen physically dissolved in plasma, the two mechanisms [illegible] oxygen by 11% (Comroe and [illegible] Basis for Oxygen Therapy, Springfield, Ill., Charles C Thomas, Publisher, 1950). Paulet attributed the beneficial effect of increased oxygen transport to augmentation of that small proportion of cellular respiration which is independent of cytochrome oxidase (the enzyme inhibited by cyanide). Even if the metabolic effect of oxygen is small, it may prolong life enough to give detoxification mechanisms (natural and therapeutic) a chance to operate.

Oxygen is a readily available therapeutic agent, and its use in cyanide poisoning should not be neglected. *Probably it should be used even after* administration of nitrites and thiosulfate, as the methemoglobinemia induced by this treatment re[illegible] blood to carry oxygen to the brain.

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FORMATION OF LIPIDS

To the Editor:—The paper by Holman, McGill, Strong, and Geer in The Journal, May 23, page 416, presents evidence for the local formation of lipids rather than filtration into the arterial bed in the pathogenesis of arteriosclerosis. The cause is ascribed to special manufacture by the local cells for lipids as well as enzyme-hormonal influence. The fatty streaking in human arteries is considered the earliest stage of the arteriosclerotic process. They, however, ignore physical causes considered by previous investigators, particularly Moschcowitz, who stressed the importance of a combination of factors of which the most important are the prolonged normal intravascular pressure plus perivascular resistance. Vascular constriction is another factor affecting local resistance. I have shown (*Angiology* 6:556-566 [Dec.] 1955) that this results in intimal proliferation followed by fibrosis, thrombosis, infarction, and gangrene—the second, third, and fourth stages according to Holman and associates. I suggested that the early pathological changes in the vessel resulted from a local ischemia due to the pressure. Whether the lipid formation resulted from this ischemia is conjectural. From the lipid streaking concentrated around the ostia of the branches of the aorta, as illustrated in the article of Holman and his group, one may reasonably conclude that lipid formation or infiltration favors areas under increased pressure and resistance.

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NOCTURNAL HABITS OF SNAKES

To the Editor:—In The Journal, May 16, 1959, pages 268 to 272, is a good article by McCreary and Wurzel on poisonous snake bites. On page 270 is a puzzling statement that "All the Crotalidae are front-fanged serpents, generally nocturnal in their habits, and usually capable swimmers."

I am in my late 60's, have lived all my life in what may be correctly called rattlesnake country, and have seen many rattlesnakes in their natural habitat. I have heard accounts of persons sleeping on the ground at night and being bitten by rattlesnakes, but I have been unable to obtain verification of any such account. Especially in this western country it has been my observation that the rattlesnake stays in the relatively cool shaded areas during the hotter portion of the day. Especially at altitudes above 2,000 ft., the nights are frequently quite cool and snakes become lethargic. I would appreciate a comment on this alleged nocturnal habit of rattlesnakes, since the quoted statement is contrary to my experience.

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The above comment was referred to the authors of the article cited, and they have submitted the following reply.

To the Editor:—Mr. Roger Conant, curator of reptiles at the Philadelphia Zoo, tells us that most of the rattlesnakes in the humid East and Southeast become nocturnal during very hot weather. They remain hidden during the daylight hours and do their prowling and hunting after the ground and air have cooled. The situation is somewhat different in the arid regions where the temperature rises very high during the daylight hours, especially when there are no clouds. In these regions temperatures tend to drop considerably at night, and this is especially true at higher altitudes. Nocturnal temperatures in these areas may be too low to stimulate the snake into activity. However, Mr. Conant tells us that the herpetologists who live in the West say that it is most unusual to find rattlesnakes about at any time of the day except in the spring of the year when they have recently emerged from hibernation, when they are hungry, or when the mating instinct is strong and when temperatures in the sun are not too severe. We would assume that much of Dr. Schaefer's experience with rattlesnakes has been in such arid country.

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MISCELLANY

RETIREMENT CRITERIA FOR PHYSICIANS

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Dissociation from medical practice, with its implications of retirement and leisure for the physician, presents a problem that has been discussed too infrequently in our medical journals. Yet it has become a dominant conversational topic among colleagues in hospital lounges as well as interdepartmental and intradepartmental staff members of our institutions for medical teaching. The majestic attraction of the word "retirement" approaches in popularity the term "baseball" in gatherings of seasoned physicians; their conversations are frequently threaded with attempts at solution. Indeed, free discussions concerning retirement have their embryonic origin not infrequently at such early stages as the resident training period.

Usually before middle age, and sooner rather than later, the physician becomes confronted with the problem of desire for voluntary separation from professional duties, assuming he survives long enough. As life expectancy has become lengthened, more physicians face the decision of retiring voluntarily. Today's influences on the industrial worker, the corporate executive, and the organizational employee are each receiving extensive sociological study concerning their retirement problems. Research studies applicable to the intrinsic pressures on our medical member groups have been deprived of parallel investigation or attention. It should suffice to point out that physicians affiliated with medical educational and veterans' facilities; the departments of the Army, Navy, and Air Force; and medical departments of industry, in many instances, retire mandatorily at a fixed age, usually 65 years. Hence the even greater importance of the problem when applied to the self-employed and unregimented individual practitioner or specialist.

Are there basic criteria, direct or implied, that should apply to careful short-range or long-range planning for retirement? What might they be? Should our thinking be schooled in a philosophy toward this end? And can one justifiably enumerate a few fundamental, nontheoretical reasons for separating oneself from the wear and tear of application to patient care? Should the selfish interests of oneself and dependents, after prolonged educational and specialized training periods, influence one's decision?

Answers to these questions require medicosocial investigation into today's society, in the conservation of our store of specially trained manpower, and in the "carnival of economic change." Attempts on the part of the individual doctor to resolve his personal basic requirements leave him confused, insecure, and engulfed by "the doctor's dilemma." Common sense dictates that a plan be designed to provide comfort in retirement for the physician and his family. In essence his spiritual, mental, physical, and financial prerequisites must be satisfactorily fulfilled. Preparations excluding these provisions lead to pathetic degenerative parasitism not alone for the physician but equally shared by his dependents.

Let us divert our thinking for the moment from leisure substitutes, programs for retirement, and those philosophical and compensatory pleasantries which may precede or follow cessation from active practice, and confront ourselves with a few of the basic criteria for retirement.

Proverbial Routine

Unfortunately, soon after launching into active practice, the enthusiastic young physician, conscientious, forthright, and usually married and with dependent children, begins to establish a "way of medical life." Customarily, this pursues a day-to-day pattern, relatively invariable, which with seasoning and maturity inadvertently blends into a characteristic over-all repetitiousness. In due time, varying degrees of deviation from this rather set "design for professional living" produce irritability toward his family, inducing an obvious restlessness of manner and often developing into an intermittent feeling of "internal jitters." By contrast, however, a conscientious stability with external charm, warmth, and gentleness toward patients always appears on the surface, evidenced by the physician's well developed and stylistically accomplished art of handling patients.

Thus with longevity in practice, exposed as it is to fluctuant influences, there develop deep, conflicting urges to divorce oneself from medical work. This may well approach a status inconsistent with the maintenance of smooth, balanced, and integrated behavior which is required by physical, mental, and emotional demands. Such wavering compulsiveness, once established, points toward the need for retiring. Should this compulsive determinism remain unbroken, it likens the physician to a soft-shelled crab exposed to a shark; and involuntary retirement becomes imminent. This need for separation from professional duties becomes conclusive when test instances of repeated vacations fail to alleviate the compulsion.

Predisposing Tensions

In contemporary medical practice, whether institutional, industrial, or individual, subjective pressures, either intermittent or sustained, are invariably present. These may be termed intangible pressures and may be enumerated: competitive influences, hurried medical life, desire for making and sustaining professional and other contacts, civic activities, social impositions of family life, and religious participation. Of perhaps even greater import is the universal problem of a physician's becoming overtaxed by patient load; and, more important, his dedication dictates that he play the role of "Lord Bountiful" to their abundant and varied personal problems. Other pressures are too numerous to relate. Their cumulative sequelae over the years, despite the transient forgetfulness and dilution afforded by relaxation and infrequent vacations, precipitate uncontrolled inner tensions. Should these tensions rise above the level of the physician's subconscious, they disturb his behavior pattern. Frequently objective behavior changes are detected by his colleagues and eventually become apparent to members of his family. Uncontrolled tensions, sustained and manifest, are of paramount significance in determining the need for retirement.

Prophetic Planning

Men of medicine as educators, practitioners, or trained specialists become individualists and nonconformists in their thinking and in their methods as well as in their aspirations. Yet lurking in their mental recesses is a uniformity of thought concerned with the sunset of their days, far off on the visible horizon of life. Whether the young or old physician smokes a pipe, cigar, or cigarette (filtered or otherwise), a plan for retirement presents one sphere of thought in which self-initiated, unadulterated, and filtered thinking must be unique and exclusive unto himself. This point I wish to emphasize and make unmistakable.

The planning of a retirement program cannot begin too early in the life of the practicing physician. Formulation of a prudent, adjustable arrangement, within the framework of an established program, is not only desirable but essential to our changing times. Nevertheless, flexibility within a program adaptable to current changing personal and family conditions should be decided on free from contaminating influences. Conclusive advice should not be sought from medical colleagues, lawyers, accountants, bankers, insurance or stock brokers, estate analysts, and consultants, nor, above all, from successful acquaintances and patients. One's projected plan should be constructed on one's own thinking and by oneself alone. (Naturally, this statement should not be construed to exclude periodic and frequent discussions between the physician and his wife or other vitally concerned members of his family. It also does not preclude a full understanding and familiarity with reliable source material on all forms of investments, such as insurance, real estate, stocks and bonds, and business investments.) Fewer errors of judgment compatible with one's ultimate needs are likely to occur.

The physician alone is cognizant of the interplay of his emotional, social, economic, and familial requirements. Not only for the present but also for the future must he assert an imaginative daring in planning fulfillment of his varied needs. Because the physician and his family are to become the recipients of benefits derived from such an attitude, he must remain a consistent thinker. His lack of prior business training and acumen presupposes that he now develop new initiative and creativity. A term well suited for such a premeditated plan as described, I like to think, is "organic planning with flexibility." To better understand and appreciate "organic planning with flexibility" let me paraphrase and interpret. In principle, one's program should not be composed of separate and unrelated forms, fragments, or parcels of investments, but rather it should be a plan in which each and every investment is likely to appreciate and grow logically as a consequence to prior ones. Such planning should possess adequate diversification and be amenable to reanalysis and reevaluation, since from time to time new and added personal requirements occur.

Once established, a program should be adhered to with tenacious loyalty, free from divergence and manipulation with a speculative tinge. Patient long-range fidelity to a carefully selected program will yield for the physician pride of accomplishment, enhancement of content, and a paradoxical improvement for solving old and new problems.

Perception and Conditioning

Assuming a flexible and organic retirement program has been patterned to his needs, the physician should begin to anticipate his expected severance date from practice. This should be established sufficiently in advance to allow him to prepare himself. Essentially when should such preparation begin, and in what should it consist?

Adequate security from financial returns, undoubtedly basic and essential, is of no greater importance to the physician than the conditioning of his outlook and thinking after actual cessation from medical practice. The amount of time to spend on such preparatory effort not only is distinctly individual but should result exclusively from personal soul-searching and self-analysis. Progress along this line is slow and often discouraging. However, for practical purposes, no less than several months to two years or longer should be spent on this matter in advance of the projected date of retirement.

A detailed and analytic outline of the characteristic intricacies and peculiarities of the physician's way of life in practice must be carefully thought out. This is as diverse as the many races, cultures, personalities, and folkways comprising the fundamental moods, moral views, and customs of any group. This can and must be accomplished by the physician with little outside help, preferably on his own and through persistent effort. The younger the retiring physician the easier it becomes for him to establish with facility a contented attitude toward his expectations on his retirement. The more completely one can detach his emotional attitude from his practice the better is he conditioned for retirement. Let me assure you that any degree of discontent experienced after retirement from active practice will be fleeting, despite one's apprehensiveness. The ultimate attainment of proper adjustment is wholly dependent on conquering and eliminating certain attitudes toward oneself, family, and patient acquaintances. The periodic essays appearing in The Journal in the "Leisure Corner" department have been beneficial from this point of view.

Leisure Substitutes

Customarily, the newly retired person faces a brief transitional period after cessation from prior activities. As a former practitioner one is usually dismayed and bewildered in spite of the apparent perfection with which he is conditioned to his new anticipations. With courage he should be ever conscious of the presence of a silvery lining beyond each seemingly endless but passing cloud.

Generally, the physician has made plans for a brief or prolonged vacation to forestall this period. There may or may not be a preplanned removal of his family to begin a new life in an entirely new place. Whatever the selection, the once feverishly occupied life of a doctor must become transformed into a tranquil, unrepressed new life.

The diverse activities which intelligent members of our profession can choose are too numerous to tabulate. Blessed with wisdom and interesting temperaments, our colleagues are fit for any one of many leisure substitutes. One may choose among indoor and outdoor activities, cultural enjoyments, travel interests, civic and club participation, medical research, reading, writing, religious activities, and a family togetherness heretofore but incompletely enjoyed. The adoption of any one or more of these as a pastime will offer companionship and camaraderie that will become enjoyably time-consuming; and, above all, the physician will enjoy a general well-being, emancipated from his professional concerns.

For you, yesterday's and today's sameness of life in medicine will move unruffled into tomorrow's bountiful life. As an advisor to sufferers of mankind, countless blessings can be yours for the seeking; for what seemed a difficult challenge now becomes eased by gracious acceptance. To you will be offered contentment and serenity as a new and hopeful paradise unfolds.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Diuretic Effect of Steroid Therapy in Obstinate Heart Failure. J. N. Mickerson and J. Swale. Brit. M. J. 1:876-883 (April 4) 1959 [London].

The authors report on 4 men and 9 women, between the ages of 41 and 82 years, with refractory congestive heart failure who were treated with prednisolone at the Charing Cross Hospital in London. Clinical observations suggested an initial coexistent endocrine overactivity followed subsequently by adrenal cortical insufficiency. This premise was supported by the presence of hyponatremia, a normal or elevated serum potassium level with an increased blood urea in these patients with chronic heart failure, which had become resistant to therapy with digitalis, a low-salt diet, and diuretics. The urinary excretion of 17-ketosteroids was estimated in 4 of these patients, and in 2 the corticoid excretion was also assessed. Subnormal values were obtained in each patient, and in one they were consistent with a diagnosis of Addison's disease. After administration of corticotropin the urinary excretion of these adrenocorticoids increased in each patient and was accepted as evidence that hypoadrenocorticism was due to failure of the anterior pituitary rather than to adrenal cortical failure.

Replacement therapy with prednisolone given in doses of 5 mg. 3 times a day for the first 24 to 48 hours, followed by a maintenance dose of 2.5 mg. 2 or 3 times daily, greatly enhanced response to diuretics in all 13 patients who received this treatment. All were relieved of congestive heart failure and also, when coexistent, of left ventricular failure. Two patients died of pulmonary embolism after 1 and 2 weeks of prednisolone therapy respectively. These results, considered in conjunction with those previously recorded in patients with congestive heart failure, suggest a pattern of events contributing to the formation of edema. The pituitary-adrenal mechanism, already fully extended in response to congestive failure, becomes exhausted, antidiuretic hormone overactivity persists, and water retention occurs, with resulting tissue fluid hypotonicity. It is unlikely that the diuresis induced by prednisolone was due to increased urinary loss of sodium, since all the patients had a decreased serum sodium level before the institution of steroid therapy, and the serum sodium concentration increased and remained at a normal level despite a profuse diuresis. It must, therefore, be assumed that the increased urinary output was due to a predominant water diuresis. Parallels are drawn between the edema of late-stage congestive heart failure, nephrotic edema, and starvation edema.

Streptococcal and Non-streptococcal Sore Throat. V. Esmann. Acta med. scandinav. 163:265-276 (no. 4) 1959 (In English) [Stockholm].

Sore throat is a frequent symptom in several common acute infections, such as streptococcic infections of the pharynx, diphtheria, mononucleosis, Vincent's disease, influenza, or primary atypical pneumonia. In addition, the group of so-called undifferentiated acute respiratory diseases sometimes presents a clinical picture which may readily be mistaken for a streptococcic sore throat. It has been demonstrated that the new virus group (adenovirus) is responsible for a large proportion of these cases. In an attempt to elucidate how often such infections are due to beta-hemolytic streptococci or how often they may be ascribed to other causes, the author made studies on 81 patients who were acutely ill, with a sore throat as the predominant symptom. The series originated from the clienteles of 20 general practitioners. Pharyngeal material was obtained by rubbing a sterile cotton swab against the tonsils, the soft palate, and the oropharynx. The streptococci were identified by their colonial morphology and their ability to produce beta-hemolysis on blood-agar plates. Both doubtful and typical colonies of streptococci were isolated and studied for group and T antigens. The antistreptolysin titer (AST) was determined by the method of Kalbak. The antistreptococcic-hyaluronidase titer (ASH) was determined at the Danish State Serum Institute by the turbidimetric method of Faber.

Growth of streptococci was obtained in 34 (or 42%) of the patients. An increase in AST was found to be a significant sign of streptococcic sore throat, when this increase amounted to 100% of the initial AST, and when the convalescent-phase titer exceeded 1:100. An increase in the ASH was found to

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The place of publication of the periodicals appears in brackets preceding each abstract.

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be a significant sign of streptococcic sore throat, when the convalescent-phase titer exceeded 1:9000. A significant increase in one or both antibodies was revealed in 62% of the patients. A significant increase in the antibody formation against adenovirus occurred in 3 patients with sore throat, and a questionable increase was seen in 1 patient. One of the significant increases occurred in a patient with mononucleosis who may have had a superimposed adenovirus infection. The Paul-Bunnell test showed definitely increased titers in 6 patients with sore throat, who all revealed hematological findings characteristic of mononucleosis. Smears of necrotic tonsillar tissue from 2 patients with Vincent's disease showed fusiform bacilli and spirilla in large numbers. Forty-four per cent of the 81 patients with sore throat had to be classified as having undifferentiated respiratory disease. Like most other investigations this study showed that streptococcic and nonstreptococcic sore throat cannot be differentiated on the basis of clinical observations, except that the absence of redness of the fauces suggests that the case is of nonstreptococcic origin. The bacteriological study of pharyngeal flora not only is of great diagnostic importance but also is a valuable aid for therapy.

Survival in Acute Myocardial Infarction: Factors Observed in 318 Patients. E. E. Harnagel, V. V. Jelinek, A. A. Andonian and C. W. Ulrich. California Med. 90:264-267 (April) 1959 [San Francisco].

Factors influencing mortality were studied in 318 patients with acute myocardial infarction, admitted to the California Hospital in Los Angeles during 1949-1951. There were 228 men and 90 women, ranging in age from 33 to 86 years. The average age of the men was 60 years, and of the women 65½ years. The mortality in women was 44.4%, in men 39.5%, and in the total series 41%. The death rate increased with the age of the patient. Twenty-six per cent of all deaths occurred within the first 24 hours, 44% within 72 hours, and 71% within the first week after hospital admission. Increased mortality rate was associated with previous history of congestive failure, myocardial infarction, hypertension, or cardiomegaly. Among the circumstances immediately preceding infarction, only surgical operation or massive hemorrhage (usually gastrointestinal) appeared to influence the outcome. Not only the presence but also the degree of shock, congestive heart failure, cyanosis, and dyspnea adversely influenced the chances of survival. Duration, location, radiation, and number of attacks of pain did not seem to be associated with extraordinary mortality rates. Patients with anterior infarction, particularly if it occurred at the septum, had the poorer prognosis. The prognosis was likewise poor in those with combined anterior and posterior infarctions. Thromboembolic complications and certain disorders of rhythm and of conduction definitely worsened prognosis. The authors emphasize the necessity of classifying acute myocardial infarction for prognostic purposes, which not only would increase knowledge of the history of the disease but also would supply valuable control data for future investigations of therapeutic agents.

Reversal of Tuberculin Reaction in Early Tuberculosis. J. M. Adams, V. A. Kalajan, B. O. Mork and others. Dis. Chest. 35:348-356 (April) 1959 [Chicago].

The authors report on 160 persons with a previous negative reaction to the tuberculin skin test, in whom the reaction turned to positive (converters). They were divided into 3 groups: Thirty-five (group A) were infants, aged less than one year, who were assumed to have had a previous negative skin reaction because of their age; 87 (group B) were persons who had turned from negative to positive within 3 months; and 38 (group C) were those who had done so within 12 months. Of the 160 persons, 121 (28 of group A, 69 of group B, and 24 of group C) were then followed by repeated tuberculin tests for signs of change in their reactions to the tuberculin tests. Sixty-eight (56%) of the 121 persons showed a change in their skin reactivity from a positive to a negative reaction (reverters). Of these 68 persons, 17 (60%) belonged to group A, 40 (58%) belonged to group B, and 11 (46%) belonged to group C. By arranging the 68 persons according to the degree of their skin reactivity, it appeared that the ratio of reverters was 76% among those with a reactivity of 1+, 50% among those with a reactivity of 2+, 38% among those with a reactivity of 3+, and 17% among those with a reactivity of 4+.

The reasons for this surprisingly high rate of change are unknown, but it may represent early detection of tuberculous infection in persons who might otherwise go unrecognized at this stage of their disease. By repeated skin testing of persons with known negative and positive reactions to the tuberculin test, the natural history of tuberculosis may become better understood. Roentgenologic studies were performed on 97 persons in this series and revealed a direct relationship of the findings with the degree of change in tuberculin reactivity. The persons with negative chest roentgenograms showed a high rate of reversal; in contrast, no change in skin reactivity was found when the roentgenologic findings indicated a "presumably active" lesion.

When guinea pigs, inoculated with strains of mycobacterium tuberculosis, were treated with isoniazid, their skin reactivity to tuberculin was reduced as compared with that of untreated control animals. If treatment was begun at the time of inoculation, some animals failed to have a positive reaction, and all had negative cultures. If treatment was delayed, all had positive reactions to the skin test, and a few showed signs of tuberculosis at autopsy and by culture.

The Incidence of Cancer in Chronic Leukemia and in Polycythemia Vera. J. H. Lawrence and W. G. Donald Jr. Am. J. M. Sc. 237:488-498 (April) 1959 [Philadelphia].

A review of the literature and of a series of cases of primary malignancy occurring in patients with chronic lymphatic leukemia, chronic myelogenous leukemia, and polycythemia vera suggests an increased incidence of cancer in these conditions. In leukemia, there is no indication from reported cases of a predilection for any specific organ or system. With polycythemia vera, however, there is a high incidence of renal malignancy—17 cases in 630 patients; but aside from the kidney no apparent close association with an organ has been observed. The role of radiation therapy in the production of associated malignancies is not clear. In the authors' own series and in other reported series of patients with polycythemia vera, there has been no indication of an increase in malignancy in the radiation-treated group as opposed to the group treated by other methods, but the number of patients is not large enough for adequate comparison. No series of untreated patients with leukemia is available for analysis, but in the experience of the authors and in reports in the literature there is no indication that radiation in these patients has produced malignancy. In agreement with the experience of others, the authors found that patients with polycythemia vera and with chronic leukemia have an increased susceptibility to malignancy, but this susceptibility is not produced by radiation therapy.

Phenethylbiguanide in Diabetic Patients: Clinical and Metabolic Effects. T. H. Lambert. California Med. 90:257-260 (April) 1959 [San Francisco].

A new nonsulfonylurea, hypoglycemic compound, phenethylbiguanide (N'-betaphenethylformamidinyliminourea hydrochloride [DBI]), was given orally to 70 unselected and nonobese patients with diabetes mellitus. There were 34 males and 36 females, ranging in age from 6 to 84 years. The patients were studied for periods which varied from 7 days to 16 months; 53 were hospitalized, and 17 were outpatients. Their diabetic condition had existed from 1 year to 29 years, the average duration being 10.6 years. All the patients had been observed while being treated by diet alone, or by diet and insulin. The dosage of phenethylbiguanide varied; adults were given at the beginning 150 mg. and children 75 mg. of the drug in divided daily doses. An adequate control of diabetes was obtained with phenethylbiguanide alone in 27 patients, ranging in age from 40 to 73 years. These patients required 50 to 225 mg. of the drug daily. In 10 of them side-effects, such as anorexia, nausea, vomiting, or diarrhea, appeared 1 or 2 weeks after treatment was started. These effects subsided in some despite continuation of treatment, and in others after a temporary reduction of the dosage.

Treatment with phenethylbiguanide was discontinued in 12 patients because of untoward manifestations attributed to ketosis or to irritation of the gastrointestinal tract or to some unknown cause. Whether the phenethylbiguanide tablets were given before, during, or after the meals, or whether antispasmodics or antacids were given before or after the drug did not seem to influence these unpleasant symptoms. A more stable control of diabetes was maintained in 11 patients with the combined administration of phenethylbiguanide and insulin. Two patients in whom the disease was well controlled were lost to observation, and in 18 the drug had no demonstrable hypoglycemic action. However, no evidence of serious toxicity was demonstrated in clinical and metabolic studies; there was no impairment of liver or kidney function; and no changes were seen in repeated hematological studies after the administration of phenethylbiguanide.

The Primary Mortality and the 5-Year Prognosis of Cardiac Infarction: A Study Which Considers in Particular How the Prognosis Is Affected by the Composition of the Material as Regards the Age and the Sex of the Patients and the Severity of the Infarction. S. Helander and M. Levander. Acta med. scandinav. 163:289-304 (no. 4) 1959 (In English) [Stockholm].

This report is concerned with 286 patients, 173 men and 113 women, who were treated for their first attack of cardiac infarction at the Karolinska sjukhuset, Stockholm, during the years between 1940 and 1949. The aim of the investigation was to study some of the factors in the composition of the case material which could influence the primary mortality and the long-term prognosis of patients with cardiac infarction. For this reason the patients were classified with regard to age, sex, and severity of the first attack of myocardial infarction. As regards the severity of the attacks, patients showing the clinical picture of shock, with a marked fall in blood pressure in the first days of illness, were classed under group 1. Those manifesting no shock but otherwise presenting the complete picture of cardiac infarction, with fever, raised erythrocyte sedimentation rate, and leukocytosis, were classified as group 2. Those with milder cases, in which only electrocardiographic tracings showed evidence of cardiac infarction, were classified as group 3. The primary mortality was 54% in group 1, 27% in group 2, and 4% in group 3. The difference in the primary mortality in relation to age and sex of the patients was most clearly marked between the older and the younger women (48 and 6% respectively). It was postulated previously that women have a higher mortality than men; this seems to apply to older women only.

For the estimation of the 5-year survival rate, the authors had at their disposal the records of 232 patients. Fifty-eight per cent were still alive after 5 years. The severity of the infarction did not influence the continued course as markedly as it did the primary mortality (50% survivals in group 1 against 62% in group 2; the difference is not statistically significant). It is noteworthy that in group 3 the 5-year survival rate was as low as 42%. The difference in the primary mortality between the younger and the older women was not matched by a similarly marked difference in the 5-year survival rate (62 and 49% respectively). A comparison between the 5-year survival rate of patients after the first attack of myocardial infarction, on the one hand, and of the population of Stockholm of a comparable age, on the other hand, showed a markedly increased mortality among the former. There was thrombosis in the coronary artery in 42 of 80 cases studied at autopsy, and coronary embolism in 1 case.

The electrocardiographic records and the postmortem findings showed good correlation with regard to the localization of the infarction. Electrocardiographic evidences of atrioventricular and of intraventricular heart block were indicative of a poor prognosis, inasmuch as these patients had a primary mortality of 69%, compared with 23% for patients in whom electrocardiographic tracings did not show such changes. Of 135 patients who survived 5 years after the infarction, 85 were still alive an average of 8½ years after the primary infarction. Examination of 78 of these patients revealed that 21 could maintain a normal activity, 34 had a lowered capacity, and 23 were invalids. Fifty-four patients were troubled by angina pectoris, but it was mild in 9 of them.

Kartagener's Syndrome in Identical Male Twins and a Female Sibling: Report of Cases, with Comments on Pathology and Familial Manifestations. L. S. Safian and F. B. Mandeville. J. Florida M. A. 45:1143-1148 (April) 1959 [Jacksonville].

The authors report the occurrence of Kartagener's syndrome, a triad consisting of situs inversus with bronchiectasis and paranasal sinusitis, in 2 34-year-old men who were clinically identical twins and in their 32-year-old sister. There were 4 other siblings, 2 brothers and 2 sisters, who were all reported to be in good health. The father of the 7 siblings had had diabetes and had died of a heart attack. The mother was alive and well. The bronchograms of the 3 patients showed evidence of bronchiectasis, and multiple roentgenographic views of paranasal sinuses showed clouding of maxillary antrums and other sinus groups; frontal sinuses were rudimentary or absent. All 3 patients had complete transposition of viscera. Seven other instances of family groups presenting multiple siblings with Kartagener's syndrome were collected from the literature.

The occurrence of Kartagener's syndrome is here reported for the first time in clinically identical twins. The syndrome is briefly discussed in some of its pathological and clinical aspects. The seriousness primarily of the bronchiectasis is stressed, and the importance of its early recognition among patients with visceral transposition is emphasized. The factor of familial occurrence is pointed out.

Diagnosis and Treatment of Acute Renal Failure: Experience from a Series of 56 Consecutive Cases of Acute Anuria. A. P. Skouby. Acta med. scandinav. 163:277-287 (no. 4) 1959 (In English) [Stockholm].

The underlying mechanisms of acute renal failure (shock kidney) are inadequately understood, and the results of treatment have been poor. Shock kidney was defined by Swan and Merril in 1953 as "the clinical syndrome resulting when renal excretory function is rapidly, but temporarily, lost because of alterations in renal circulation and the development of disseminated areas of renal tubular degeneration." The results of studies of 56 patients with acute anuria suspected of having shock kidney are presented. In 37 of these patients shock kidney was demonstrated. A diagnosis of chronic renal disorder was established in 13 of the remaining cases, while electrolyte disturbances and occlusion of renal arteries or urinary pathways were the cause in 6. In 5 of the 37 patients, oliguria was of short duration, and regulation of fluid intake was sufficient, but special therapeutic measures were necessary in 32. In 22 of these patients with an increase of blood urea value to at least 400 mg. per 100 cc. or of plasma potassium level to at least 7 mEq. per liter, indications for hemodialysis existed. It was performed 16 times in 11 patients. In patients requiring special treatment, the primary disorders often persisted and were the chief cause of death in those who died.

The main problem in patients with acute anuria is to distinguish whether oliguria is caused by a primary renal disorder or acute renal failure. Renal biopsy is useful, but complications may occur. Furthermore, acute renal failure as the cause of oliguria does occur in patients with chronic renal disease, as demonstrated in one of the present cases with chronic pyelonephritis and hydronephrosis of the right kidney, whereas in the left only lesions characteristic of acute renal failure existed. Evidence indicating that the limb lead electrocardiogram may be of diagnostic value in the differentiation between primary renal disorder and shock kidney was obtained by the author in 1957, and this was strengthened in the present study. In the patients with acute renal failure a positive after-potential was demonstrated in the limb lead electrocardiogram of two-thirds of the patients at a time when no other influence known to produce the phenomenon was detected and the plasma potassium level was normal or elevated. In contrast, a positive after-potential occurred in uremia due to primary renal disease only under conditions known to produce a positive after-potential, such as hypokalemia, diabetic coma, and after an acute attack of renal stone colic with severe pains and vomiting.

Regarding treatment, the author says that the main problems were to abolish shock, to treat the primary disorder, to administer fluids, minerals, and food, and simultaneously to reduce as far as possible the functional tasks of the kidney. Reestablishment of the circulatory volume in shock seldom was sufficient. Therefore, arterenol infusion was used. Some patients were treated simultaneously with hydrocortisone. The diuresis increased during treatment with arterenol. It is suggested that hydrocortisone may be of value in the treatment of renal failure in patients with severe primary disorders. No ill-effects have been demonstrated. The therapeutic effects obtained are largely dependent on the basic disorders.

A Case Report of a New Serological Pattern in the Rickettsial Group. P. O. Nice and W. L. Beeken. Am. J. M. Sc. 237:474-478 (April) 1959 [Philadelphia].

The case of a 48-year-old woman presenting a rickettsial disease with unusual features is reported. The patient had been well until December, 1955, when she developed dull, persistent frontal headache. During the course of the disease, high complement-fixing antibody titers developed to epidemic typhus soluble antigen (1:1280) and Q fever antigen (1:320). Agglutinating antibodies to Proteus O X 19 reached a high level (over 1:640). No significant complement-fixing antibody titers were obtained with rickettsialpox soluble antigen, epidemic typhus antigen, murine typhus antigen, or Rocky Mountain spotted fever antigen. Serum specimens from 2 dogs in the family household were drawn 8 months after the illness in the patient and were found to have a low titer of complement-fixing antibodies to epidemic typhus soluble antigen and Q fever antigen. This serologic pattern differs from any heretofore documented. The pattern cannot be explained on the basis of any known single rickettsial disease, or even on the basis of 2 concomitant diseases, unless there was failure to develop complement-fixing antibodies to some antigens. The authors believe that this may be a previously unrecognized rickettsial disease in which the causative organism shares antigens with the agents of both Q fever and typhus.

Protracted Forms of Acute Leukosis in Adults. G. Marchal, G. Bilski-Pasquier, G. Duhamel and P. Cornet. Presse méd. 67:447-449 (March 7) 1959 (In French) [Paris].

Protracted forms of acute leukosis in adults are more frequent than is usually admitted. The authors collected the cases of 21 patients, with a survival time of from 8 to 28 months, from 2 series of cases recorded at Paris hospitals. In the first series of 84 cases, gathered at random at the Broussais Hospital from 1951 to 1958, 64 patients died in less than 8 months (56 dying within 6 months), and 20 survived between 8 months and 2 years. One patient in the second series of 22 cases, observed at the Tenon Hospital, survived 28 months. This survival of an athletically built, 23-year-old man shows the importance of health at the initial stage of the disease. Altogether, 24% of the patients survived more than 8 months, and 8% more than one year.

The quality of remissions obtained in patients with protracted forms of acute leukosis was studied from the clinical and cytological standpoints. There were good results in 45% of the cases. A lack of parallelism was noted between the hematological and the clinical conditions in remissions. In the first type of remission, there is improvement from the blood picture and medullary standpoints, but a cytological relapse occurs, accompanied by worsening of the general state, anemia, and hemorrhages. After intensive treatment the clinical state is improved, but the blood and the marrow remain leukemic. In 3 patients satisfactory health status lasted from 3 to 7 months with this type of remission. In the second type of remission, treatment seemed to check the illness, but the blood and especially the marrow remained inundated with original cells. In one patient the clinical state allowed a moderate amount of work for 5 months, and the patient survived a year despite the presence of 30 to 80 blast cells per 100 cc. in blood and marrow. The quality of remissions obtained should have as criteria the duration of survival and the resumption of social activity.

The death of patients with protracted forms of acute leukosis is not different from that of patients with the classic forms. However, sometimes these patients die unexpectedly when their blood and medullary states are reassuring. Sometimes coinciding infectious disease or hemorrhage is the cause, and sometimes a cause cannot be found. Type of treatment and earliness in application have influence. The treatment which has the best chance of prolonged action consists of repeated transfusions, massive corticosteroid therapy at the beginning (1 to 3 Gm. of cortisone per day) followed by continued maintenance therapy, and 3 to 6 months' treatment with mercaptopurine. In milder cases the massive doses of cortisone may be omitted.

Blood Pressure and Obesity. H. M. Whyte. Circulation 19:511-516 (April) 1959 [New York].

Previous surveys have shown that the height of the observed blood pressure and the degree of overweight are related, but excess weight does not necessarily mean excess fat and the possibility of error in the measurement of blood pressure due to variations in the size of the arm has not been excluded. Taking these factors into account, the author studied 100 healthy men, between the ages of 20 and 40 years. Height and weight were recorded; the circumference of the upper arm was measured; the subcutaneous fat (skinfold thickness) was measured at 3 sites (paraumbilical, over the triceps, and over the inferior angle of the scapula); the blood pressure was measured from the right arm; and the serum cholesterol level was determined. The results showed a positive correlation between blood pressure and body weight, other factors being held constant. Obesity (judged by the thickness of the subcutaneous fat) had no apparent influence on blood pressure except insofar as it affected the total body weight. Serum cholesterol concentration was related to age, but not to body weight or obesity. An increase in body weight of 28 lb. (12.7 kg.), without any change in arm circumference, was associated with an increase of 10 mm. Hg systolic and 7 mm. Hg diastolic pressure. The conclusion is that blood pressure is related to weight or bulk of the body, but not to obesity except insofar as it contributes to bulk. Cardiac output seems to be related to surface area which increases with bulk. The blood pressure rises when the augmented cardiac output is forced into an aorta that may not have increased in capacity as the body weight rose. To outgrow one's aorta might be one of the dangers of overeating.

SURGERY

Hypophysectomy for Palliation of Breast Cancer: With Especial Reference to Surgical Technique. N. L. Cobb and W. B. Scoville. California Med. 90:261-263 (April) 1959 [San Francisco].

Hypophysectomy was carried out for palliative purpose in 19 patients with cancer of the breast. All the patients had a striking subjective relief of pain after the operation which appreciably decreased their need for narcotics. Ten patients showed some objective evidence of remission. Five patients were living from 1 to 6 months after the operation; 2 of these were asymptomatic, 2 were improving, and 1 was regressing. Twelve patients were subjected to endocrine therapy or oophorectomy before hypophysectomy; 5 showed no relief, but 7, who benefited from these treatments, had both subjective and objective remission after hypophysectomy. Of the 5 patients who had no remission from either endocrine therapy or oophorectomy, one had relief of pain without objective improvement after hypophysectomy, and one had relief of pain as well as objective improvement after the operation.

The survival time after the operation averaged 19.8 months for patients who had a remission, and 2.1 months for patients who had no remission. The length of time the disease existed before hypophysectomy seemed to be related to the survival time after the operation. Patients in whom remission occurred had had cancer for an average of 4.9 years before hypophysectomy, and those without remission had had the disease for an average of 2.7 years. These facts should be considered in the selection of patients for hypophysectomy. The authors found no correlation between the results of hypophysectomy and other factors, such as age of the patient, cell type of the tumor, response to roentgenotherapy, and extent of the disease.

Surgical Treatment of Neoplastic Processes in the Third Ventricle: Observation of 143 Patients. J. Papo and R. Tritapepe. Minerva chir. 14:128-138 (Feb. 15) 1959 (In Italian) [Turin, Italy].

The authors discuss the treatment of 143 surgical patients with tumor in the third ventricle of the brain. The lesion was in the anterior portion of the third ventricle in 89 patients. The third ventricle was not visible in 21 patients. Extirpation of the tumor was attempted in 17 patients, 3 of whom were operative fatalities. Radical exeresis was performed on 6 patients, 5 of whom had the lesion circumscribed within the third ventricle. Partial resection was made in 5 patients, and surgical biopsy in 3. Operation by the Torkildsen procedure was performed on 51 patients, 9 of whom died within several weeks after the operation. Of 33 patients available for follow-up, 15 died within 5 years after the operation, and 18 are still alive, with varying survival periods up to 9 years. Results of direct surgical attack do not seem to warrant its broad application, except in instances in which such procedure is indicated on the basis of ventriculographic findings. Of 22 patients who received irradiation therapy alone or preceded in a few instances by decompression, 6 are still alive at varying periods exceeding 4 postoperative years. Most of the tumors in the anterior portion of the third ventricle seemed to have grown at a slower rate than those in the cerebral hemispheres.

Fifty-four patients had a tumor in the posterior portion of the third ventricle. Direct attack on the tumor was made in 8 patients. This procedure was subsequently discontinued because of the poor results obtained. Removal of the fluid, followed by irradiation therapy, was instituted in the remainder. Double ventriculocisternostomy by the Stookey and Scarff procedure was performed on 36 patients, 2 of whom died during operation. Of the patients available for follow-up, 13 died within 8 years after the operation, and 13 are still alive, with varying survival periods up to 17 years. Operation by the Torkildsen procedure was performed on 11 patients, 5 of whom were operative fatalities. The authors believe that the procedure of fluid removal, followed by irradiation therapy for the treatment of tumors in the posterior portion of the third ventricle, is preferable to the direct surgical attack in view of the same comparative results and less degree of operative mortality.

Pulmonary Function Changes in Bilateral Resection for Pulmonary Tuberculosis. R. C. Young, F. J. Misener, J. J. Quinlan and J. E. Hiltz. Am. Rev. Tuberc. 79:468-473 (April) 1959 [New York].

Twenty-nine patients who had had bilateral pulmonary resections of tuberculous lesions performed between 1955 and 1958 at the Nova Scotia Sanatorium in Kentville were selected for study to determine the degree of change in pulmonary function after the operation. There were 16 males and 13 females, ranging in age from 10 to 49 years. Nineteen patients had moderately advanced tuberculous disease at the time of hospitalization. The ventilation tests included the determination of minute resting ventilation, expiratory reserve volume, vital capacity, and maximal breathing capacity. These tests were performed on all but a few patients less than 3 months before the first operation and between 3 to 6 months after each of the 2 resections. The results of the ventilation tests and the clinical evaluation of this study indicate that bilateral resection of reasonable extent affects the pulmonary function to a relatively mild degree. The vital capacity was appreciably more reduced in the major resection group (21%) than in the 2 minor, less extensive resection groups (14%), and the average reduction in vital capacity for all the patients was 18%. The changes in maximal breathing capacity correlated better with the extent of resection than did those of vital capacity and showed reductions of around 17% in the major resection group in contrast to no reductions in the minor resection groups. The average reduction in maximal breathing capacity in all the patients was 5%.

The probable principal cause for reduction in vital capacity is considered to be the restrictive effect of thoracotomy. In the more extensive resection the pulmonary factors undoubtedly influenced the results, but the maximal breathing capacity was apparently unaffected by the thoracotomy factor when the tests were performed several weeks after resection. Although the tests for maximal breathing capacity are valuable, they are not infallible because of the potential sources of error connected with their performance. No correlation could be found between other factors, such as the patient's age, preexisting condition, and type of disease, and the findings in the 3 groups undergoing resection.

The So-called Tight Filum Terminale Syndrome. A. Uihlein. Minnesota Med. 42:394-398 (April) 1959 [St. Paul].

The author reports on 2 women, aged 33 and 34 years, respectively, who on their admission to the Mayo Clinic presented the symptoms of an unexplained progressive paraparesis of the lower extremities suggesting the possibility of a tight filum terminale. The filum represents the caudad portion of the spinal cord which normally becomes a fibrous strand. Inadequate differentiation of the filum during the period of body growth, with lengthening of the filum as the vertebral column descends, can exert sufficient traction on the roots of the cauda equina and the conus medullaris to produce a demonstrable neurological disorder.

In addition to weakness and heaviness of the lower extremities, the first patient had urinary and fecal incontinence. Neurological examination revealed a definite sensory loss to all modalities in the sacral rootlets, with reduced sensitivity to touch, pain, and temperature. Surgical exploration in the region of the first lumbar vertebra revealed that the conus medullaris was not located at its usual level. Laminectomy at the fifth lumbar and first sacral levels revealed that the conus medullaris was attached to the dura at the level of the first sacral vertebra. The conus medullaris had undergone degenerative changes and looked somewhat like a lipoma. Anterior to this attenuated conus was a tense fibrous band that resembled the usual filum terminale. In the course of the intervention the attachment of the conus to the dura was divided between silk sutures, and then the tight filum was likewise divided. The tissue from the area of the conus was submitted to microscopic examination and represented fatty cells and nerve fibrils. Although much of the neurological deficit will persist, a satisfactory recovery is anticipated for this patient.

The right foot of the second patient was larger than the left, and the left foot was deformed, with a talipes cavus type of alteration. Neurological examination revealed that ankle jerks were absent bilaterally. The tone of the anal sphincters was reduced, and there was definite weakness in dorsiflexion of the toes, especially on the left side. There was weakness in the abductors and sensory loss to pinprick and temperature. An iophendylate (Pantopaque) myelogram showed the common dural sac lying posteriorly against the bony wall of the spinal canal, suggesting a tight filum terminale. Surgical exploration at the level of the fifth lumbar and first sacral vertebrae and at the level of the first and second lumbar vertebrae did not reveal any evidence of a tight filum terminale. The conus medullaris appeared to be in a normal position. Convalescence of the patient was uneventful. It was felt that she probably had a congenital anomaly of the lower extremity on the left side.

It is believed that in young patients with progressive paraparesis without adequate explanation for the findings early surgical intervention might prevent irreparable progressive neurological changes by determining the presence or absence of an abnormally low-lying conus medullaris of the spinal cord or a tight filum terminale or both. Roentgenograms of the thoracic and lumbar vertebrae, as well as contrast myelography, should be included among the measures employed in this clinical problem.

Sarcomas of the Stomach. M. Oria. Minerva chir. 14:229-235 (Feb. 28) 1959 (In Italian) [Turin, Italy].

Among 328 operations for benign or malignant tumor of the stomach performed at the Main Hospital in Turin during the past 10 years, 6 were concerned with sarcoma of the stomach in patients whose ages ranged from 57 to 68 years except for one whose age was 27. There were 3 instances of reticulosarcoma, 1 of fibrosarcoma, 1 of fibromyxosarcoma, and 1 of lymphoreticulosarcoma. The tumor, not being an extensively infiltrative type in these patients, was endogastric in 4, intramural in 1, and intramural with tendency toward the esogastric area in 1. Cramp-like epigastric pain was the initial symptom in 3 patients, and ulcer-like symptoms in the others. The symptoms developed within 2 to 8 months in 4 patients and within 1 to 2 years in the other 2 before hospitalization. The course of the disease became acute after onset of the symptoms, which circumstance brought the patients relatively early to the physicians' attention. Another salient feature was the absence of a true pyloric stenosis, although the considerable size of the tumors impeded the passage of food. Prognosis seemed to be more favorable in the patients with sarcoma than in those with carcinoma of the stomach because of a better indication for surgery, less tendency to metastatize, and possibility of an earlier diagnosis and referral to surgery. One patient died a year after the operation; 2 patients were alive 2 and 3 years, respectively, after the operation; 1 was operated on very recently; and 2 could not be traced.

An early and extensive operation is indicated for treatment of sarcoma of the stomach. Patients with inoperable disease are given irradiation therapy. Lymphosarcoma is more sensitive to roentgenotherapy than reticulosarcoma; fibrosarcoma is hardly sensitive to roentgenotherapy. Preoperative differential diagnosis of sarcoma of the stomach from carcinoma of the stomach is difficult, but it is possible with the aid of clinical, roentgenologic, and endoscopic findings.

Experimental Investigations on Induced Cardiac Arrest. A. Piskorz, J. Zawilski, I. Bowbelska and S. Drozdowski. Thoraxchirurgie 6:384-389 (March) 1959 (In German) [Stuttgart, Germany].

The authors describe animal experiments on induced cardiac arrest, which aimed at comparing the toxic effects of potassium ions and of acetylcholine, because either potassium citrate or acetylcholine are generally used for the induction of cardiac arrest in bypass operations on the heart. A de Wall-Lillehei oxygenator was incorporated in the apparatus which the authors used for the artificial maintenance of the circulation. Cardiac arrest was induced in 10 dogs by the injection of acetylcholine into the coronary vessels. This resulted in a sudden transition of normal cardiac function to arrest during the diastole. Only slight rhythmical atrial contractions could be observed, and occasional ventricular contractions resulted on touching the myocardium. The return of the cardiac function took place by way of occasional contractions which gradually merged into a normal sinus rhythm.

Potassium citrate was used to induce cardiac arrest in 13 dogs. The cardiac arrest was preceded in these dogs by irregular atrial and ventricular contractions. After arrest had been achieved, the relaxation of the myocardium was complete. The return of the cardiac function passed through a phase of irregular contractions, and in 5 animals cardiac massage had to be employed in order to restore the cardiac function. In 6 of the 13 dogs fibrillar, convulsive contractions resulted, which subsided spontaneously in only 1 dog; in the other 5 dogs, another injection of potassium citrate became necessary, but fibrillation recurred in 4 of the animals and resulted in their death on the operating table.

The authors conclude that, with the use of acetylcholine, cardiac arrest can be induced during the diastole for a period of from 10 to 20 minutes without noticeable impairment of the function of the heart muscle. The transition from normal sinus rhythm to cardiac arrest in the diastole takes place almost instantaneously, and normal heart action returns with full, although at first isolated, contractions which merge into a normal sinus rhythm. Acetylcholine does not achieve complete cardiac arrest; minor atrial contractions persist, and touching the heart elicits some complete contractions. Potassium citrate achieves a more complete cardiac arrest and relaxation of the myocardium than does acetylcholine, but the potassium ions involve the danger of inducing fibrillations, which may be fatal.

The Carcinoid Neoplasm and Syndrome: A Review with Extension by Unusual Cases. L. Gonzales, D. L. Graller, J. Giuseffi and A. M. Keirle. Am. Surgeon 25:226-231 (April) 1959 [Baltimore].

The authors report 2 unusual cases of carcinoid neoplasm and syndrome in a 47-year-old man and in a 12-year-old girl who were admitted to the surgical clinic of the University of Cincinnati Medical Center. The male patient was admitted because of nausea, vomiting, and diarrhea of 6 days' duration. Weakness 2 days before admission had forced him to bed. In the last 3 years he had had similar attacks, which were accompanied by flushing of the face, shoulders, and chest. The patient had undergone a laparotomy 2 years previously in another hospital for a suspected cholecystitis, and numerous tumor nodules had been found in the liver and 2 in the omentum. No primary source of the tumor had been found in the intestine. A liver biopsy had been reported as revealing metastatic carcinoma. On the present admission, a chest roentgenogram revealed a rounded nodule in the midlung field, which was thought to represent a neoplastic lesion, with probable sclerosing lesions of the ribs. An abdominal roentgenogram revealed extensive hepatomegaly and sclerosing lesions of both the ilia and the sacroiliac joints and of the 8th, 9th, and 12th thoracic vertebrae. The urine test was strongly positive for 5-hydroxyindole acetic acid (serotonin). The patient's symptoms, characteristic flush, and 2-year history of surprising work activity after the detection of a metastatic tumor in the liver supported the diagnosis of metastatic carcinoid. A bone biopsy of the posterior iliac spine on the right revealed carcinoid tumor. The roentgenogram showing osteoblastic bone metastases was disconcerting, as osteoblastic metastases are extremely rare. The similarity of the bone biopsy to the liver biopsy taken 2 years previously and the high urinary serotonin content established the diagnosis.

The 12-year-old girl was studied for obesity. On examination an intense mottled redness of the face was seen. In the last 4 years she too had had occasional attacks of vomiting and diarrhea. The increasing awareness of the sarcoid syndrome and the patient's positive reaction to the serotonin test established the diagnosis of carcinoid neoplasm, and an exploratory laparotomy was performed. The liver was found to be tremendously enlarged, with tumor nodules. At the junction of the jejunum and ileum a stenosing lesion of the ileum was found, extending for a distance of 2 cm. and involving two-thirds of the circumference of the intestine. There was extension of this tumor into the root of the mesentery. A wedge resection of the area and biopsy of the liver were performed. Microscopic examination of the specimens revealed carcinoid of the ileum with metastases to the liver.

Forty-eight additional cases of carcinoid tumor were collected from the records of the University of Cincinnati Medical Center during the last 10 years. Eleven of these tumors were appendical in origin, 34 occurred in the small intestine, and 3 arose in the rectum. Thirty-one of the 34 tumors in the small intestine were located in the terminal ileum, 2 in the jejunum, and 1 in the duodenum. Thirteen of the 34 tumors were malignant; 9 of these were diagnosed at laparotomy and treated surgically. Follow-up of the 9 patients with these tumors showed only 2 survivors. The average survival time from the onset of symptoms was 8.2 years and from the time of diagnosis 3.5 years.

Gastrojejunal Ulcer. H. Jinich, J. Solis, A Pitol and J. Sierra F. Rev. invest. clín. 10:383-406 (Oct.-Dec.) 1958 (In Spanish) [Mexico, D. F.].

The records of 33 patients with gastrojejunal ulcer, secondary to a previous operation for peptic ulcer, who were treated at the Hospital de Enfermedades de la Nutrición in Mexico City, were reviewed. There were 27 men and 6 women who ranged in age from 30 to 60 years. The previous operation had been performed for a duodenal ulcer in 31 patients and for a gastric ulcer in 2. It consisted of gastroenteroanastomosis, alone or with vagotomy, in 16 cases and of gastric resection ("insufficient" or "ample") in the other 17. The symptoms of recurrent ulcer appeared during the immediate postoperative period in 5 patients and within an average period of 2 years in the remaining 28. The most characteristic symptom of recurrent ulcer was epigastric pain similar to that which occurred before the previous operation. Early symptoms of this recurrence gave rise later to chronic or acute perforation in 28 cases, severe hemorrhage in 12, gastric retention in 10, gastrojejunocolic fistula in 2, and malnutrition in 16.

The clinical diagnosis was confirmed by determination of gastric acidity, gastroscopy, and radiologic examination of the stomach. There was gastric hyperacidity in 25 of the 30 patients who had this examination and hypoacidity in 5. Gastroscopy showed superficial gastric lesions. Radiologic examination proved to be of value in the detection of gastrojejunal ulcer and of its complications, the radiologic sign being the crater or "niche." The radiologic picture of gastric retention due to gastrojejunal ulcer or gastrojejunocolic fistula was extremely clear. Twelve patients who did not respond to medical treatment disappeared from observation, but 19 patients had a second operation, consisting of gastric resection, alone or with vagotomy, or vagotomy, alone or with closure of the perforation and undoing of the original stoma. Ample gastric resection (Hofmeister's operation) was performed on 12 patients; 2 patients died in the immediate postoperative period (constituting 16% mortality).

Vagotomy, alone or with closure of the perforation, was performed on 6 patients, and there was no operative mortality.

The authors conclude that gastric resection, alone or with resection of the ulcerous jejunal segment, is indicated in surgical treatment of postoperative peptic ulcers; these ulcers develop in patients in whom the first operation has been a gastroenteroanastomosis, an insufficient gastrectomy, or an ample gastrectomy, which left a functionally defective anastomosis. Vagotomy is indicated in cases of gastrojejunal ulcer, secondary to ample gastric resection or to gastroenteroanastomosis, if the anastomosis functions well.

Ectopic Breast Tissue: Report of Unusual Case. C. M. Looney, S. C. Reichman and O. F. Noel. Am. Surgeon 25:219-222 (April) 1959 [Baltimore].

The authors report a 26-year-old pregnant woman with hypertrophied breasts, who was admitted to the surgical clinic of the Vanderbilt University Hospital in Nashville, Tenn., for treatment. No secretion could be expressed from the nipples, and the right breast was larger than the left. Just superior to the right nipple there was an area of erythema with tenderness and an orange-peel appearance. The vulva was normal on pelvic examination. After an unsuccessful attempt was made to aspirate the mass in the right breast, a biopsy was performed 8 days later on this mass. Microscopic examination revealed mastitis without evidence of carcinoma.

About 6 weeks later the patient returned to the Vanderbilt Hospital and stated that one month before she had noticed a small mass in the medial inferior portion of the right breast; this mass had increased in size and the night before coming to the clinic had begun to drain. On examination, the right breast was somewhat larger than the left, and both were warm and showed the orange-peel phenomenon. A mass, 2.5 cm. by 2.5 cm., was noted in the medial inferior quadrant of the right breast. There was an ulcerated area draining a clear, watery fluid. No axillary lymphadenopathy was present. Pelvic examination revealed a uterus the size of 3 months' gestation. The appearance of the vulva was not mentioned. A bilateral simple mastectomy was done. The total weight of both breasts was 28 lb. 13 oz. (13 kg.). The patient's hospital course was uneventful, and 6 months after the operation she was delivered of a normal male infant.

One year later the patient was admitted to the Nashville General Hospital. Physical examination revealed a pregnant uterus of about 8 months' gestation and bilateral vulvar masses which were of such size that it was felt they would obstruct the vaginal outlet at the time of delivery. The 2 vulvar masses were excised; on gross examination they had the appearance of breast tissue, and microscopic examination revealed well-circumscribed lobules of highly secretory breast tissue. A week later the patient was delivered of a normal male infant.

Ectopic breast tissue may occur at any location along the milk line extending from the axilla to the medial surface of the upper thigh. The incidence of occurrence is from 1 to 2%, and such tissue may be either unilateral or bilateral. Due to the rare occurrence of malignant change, these masses give the impression of being relatively harmless. When malignant changes do occur, the prognosis is poor because of the proximity of regional lymphatics. Breast tissue occurring in the vulva unilaterally, though reportedly rare, is not too uncommon. A careful review of the literature revealed only 3 reported cases in which breast tissue was found in the vulva bilaterally. The 4th such case is reported by the authors.

Lipid Mobilization as a Consequence of Surgical Stress. C. J. D. Zarafonetis, J. Seifter, D. Baeder and J. P. Kalas. Am. J. M. Sc. 237:418-433 (April) 1959 [Philadelphia].

The effect of surgical stress on the plasma concentration of lipid mobilizer hormone and on the plasma lipids was investigated in 26 patients during the course of various operative procedures at the Temple University Hospital in Philadelphia. Lipid mobilizer hormone assays, cholesterol and fatty acid determinations, and paper electrophoretic patterns of lipoproteins were made on blood specimens obtained from the antecubital vein before and 4 hours after the operation. Similar tests were performed on samples taken from the omental artery and the omental vein at the beginning and at the end of intra-abdominal procedures. The most important findings and their implications may be listed as follows: 1. Evidence was obtained that lipid mobilizer hormone is released during surgical stress. 2. This release leads to mobilization of triglycerides from the omental depot. 3. There is a marked shift in paper electrophorograms from alpha-lipoprotein to beta-lipoprotein predominance in the omental vein blood during surgery. 4. The omentum not only responds actively to endogenous lipid mobilizing hormone with an outpouring of the aforementioned lipid components, but also appears to remove cholesterol from the blood circulating through it. 5. The lipid changes which may occur in the peripheral blood during surgical stress reflect the foregoing events as well as the capability of the liver to metabolize the lipids presented to it. The authors believe that these observations, made on patients undergoing the stress of surgery, permit delineation of a physiological mechanism in man for the acute mobilization of lipids to the liver.

Surgical Treatment of Cardiospasm. E. Hasche and H. Schubert. Thoraxchirurgie 6:434-457 (March) 1959 (In German) [Stuttgart, Germany].

The clinical picture of cardiospasm has been described under such terms as "achalasia or dystonia of the esophagus" and "dilatation of the cardial portion of the esophagus." This functional obstruction of the cardia has been ascribed to incoordination of the opening reflex of the cardial portion of the esophagus, which, in turn, has been ascribed to degeneration of the ganglion cells of Auerbach's plexus. The authors report their observations on 50 patients with cardiospasm observed at the surgical university clinic of the Charité in Berlin during the last decade. A psychological component played a significant part in the production or the exacerbation of many cases of cardiospasm during the difficult after-war period. A psychological trauma could be established as the eliciting factor in 16% of the patients. The diagnosis often proved difficult. A megaesophagus was sometimes mistaken for a mediastinal tumor, and in young persons bronchiectasis was sometimes suspected. The fact that cardiospasm may accompany esophageal or ventricular fundus carcinoma constitutes another difficult factor in diagnosis.

Treatment should always begin with conservative measures. Psychotherapy and removal from conflict situations proved helpful in all 6 patients in whom these measures were tried. Medicinal therapy and dietetic measures were effective in 14 of 16 patients. Nonsurgical dilation or spreading of the cardia by means of dilating sounds was tried in 16 patients. It was effective in 7, ineffective in 5, and caused complications in 4. Three of these 16 patients died of suppurating mediastinitis brought on by instrumental perforation of the cardia.

The main portion of the paper is concerned with the surgical treatment of cardiospasm, which was employed in 12 of the 50 patients. In all except one the cardiospasm had existed for many years (5 to 37). Myotomy was performed on 4 patients, anastomosis on 4, and resection on 4. The late results are analyzed. On the basis of clinical, roentgenologic, and esophagoscopic follow-up examinations, the authors discuss the sequels that result from esophagogastrostomy and resection of the cardia, particularly reflux esophagitis and cicatricial stenosis. Cardiomyotomy according to Gottstein-Heller proved to be the best surgical method. This operation is technically simple and relatively safe, and it preserves the physiological conditions. It does not destroy the valve and closure mechanism between esophagus and stomach, and as a result it is not complicated by gastroesophageal reflux with its serious sequels. These favorable results of cardiomyotomy were corroborated by a review of the literature, in that it demonstrated successful results in 90% of about 800 cases.

Cancer of Pancreas: Symptomatology and Therapy. H. Prydz. Tidsskr. norske laegefor. 79:252-256 (March 1) 1959 (In Norwegian) [Oslo].

Forty-two patients, 28 men and 14 women, aged from 34 to 77 years, with cancer of the pancreas and cancer of the duodenal papilla, were treated in the Drammen (Norway) Hospital from 1946 to 1958. Laparotomy was performed in 28 cases. About two-thirds of the cases were localized to the head of the pancreas. Differentiation between cancer of the head of the pancreas and cancer of the duodenal papilla is often possible only on microscopic examination. The extent of the cancer may be difficult to evaluate because of secondary pancreatitis. Besides the rare sarcoma, malignant tumors in the pancreas include adenocarcinoma, cystadenocarcinoma, and islet-cell tumor. Adenocarcinoma is frequent and is the most malignant. In the 22 cases examined histologically, the diagnosis was adenocarcinoma; in 4 cases the cancer developed from the duodenal papilla. In 16 cases the symptoms were gastrointestinal; in 11 there were symptoms from the liver and biliary tract; and in the remaining cases there were various other pancreatic symptoms. The frequency of affection of the biliary tract is ascribed in part to secondary changes due to obstruction of passage by the tumor. The possibility of early diagnosis is still slight. Courvoisier's law is of little help in practical diagnosis. A positive roentgen-ray finding is a strong indication that the tumor cannot be operated on radically. Exploratory laparotomy showed 10 patients to be unfit for formation of an anastomosis. In 14 cases palliative anastomosis was formed between the biliary tract and the intestine, and in 14 cases Whipple's operation was performed. Of the 14 patients operated on by Whipple's method, 8 died postoperatively, with the picture of shock, hepatic coma, and hyperpyrexia. The results were somewhat better in the palliative anastomosis operation—2 out of 14 patients died postoperatively.

NEUROLOGY & PSYCHIATRY

Facial Paralysis in Poliomyelitis: Report of 3 Patients with Unusual Delayed Paralysis. I. C. Sherman and S. J. Kimelblot. Neurology 9:282-287 (April) 1959 [Minneapolis].

The records of all patients diagnosed as having poliomyelitis at Michael Reese Hospital, Chicago, during 1952-1956 were reviewed. Of 407 patients with poliomyelitis, 267 had some form of paralysis. Of these, 203 patients had paralysis involving only spinal musculature; in 64, musculature supplied from the brain stem was involved. Of the 64 patients with bulbar involvement, 34 had some type of facial involvement. Thus, approximately 50% of patients with bulbar involvement had facial paralysis, while, of all 267 patients with paralysis, the face was involved in 12.7%. The incidence of facial paralysis in all 407 patients diagnosed as having poliomyelitis was 8.3%. A tabulation of cases according to years revealed great variation in the incidence of bulbar cases in any one year, even though the proportion of paralytic to nonparalytic cases did not vary widely. Facial paralysis was the only sign of bulbar involvement in 4 patients, although these individuals also had evidence of spinal cord involvement. Only 1 of the 34 patients with facial paralysis could be said to have an isolated facial paralysis in that he had no other evidence of bulbar or spinal involvement.

Facial paralysis in poliomyelitis nearly always appeared within one day of the appearance of paralysis in the bulb or elsewhere. Descriptions were given of 3 patients in whom unusual delay in appearance of facial paralysis occurred. One was a woman with bulbospinal disease in whom bilateral facial paralysis developed 11 days after the palatal weakness appeared and 6 days after she had become afebrile. At that time, she still had 18 cells per cubic millimeter and 138 mg. of protein per 100 cc. in her spinal fluid. The second patient was a man in whom a left-sided facial paralysis developed 10 days after the appearance of weakness of the left side of the palate, vocal cord, and pharynx, and 1 day after he had become afebrile. His spinal fluid was normal at this time. The third patient was a young man who had right-sided palatal weakness and 10 days later (3 days after becoming afebrile) paralysis of the left side of his face. At this time he had 25 cells per cubic millimeter in his spinal fluid. All 3 of these patients recovered completely from signs of palatal, pharyngeal, and facial weakness.

Imipramine (Tofranil): A New Drug for the Depressed. H. Azima. Canad. M. A. J. 80:535-540 (April 1) 1959 [Toronto].

A new drug, imipramine (Tofranil), was given a trial in 100 consecutive patients manifesting symptoms of depression and seen either as outpatients or in an open psychiatric setting at the Allan Memorial Institute in Montreal. There were 30 men and 70 women, with an average age of 49 years. Of the 100 patients, 38 were neurotics, 6 were hypochondriacs, 8 had mixed states including anxiety, depression, hysterical and obsessive compulsive features, 4 were alcoholics with depression, and 44 had psychotic depressive states. Imipramine was administered orally to all the patients. The average effective dose was 100 mg. daily; the optimal initial dose was 75 mg. daily, which was increased to 150 mg. within 7 days if no cumbersome side-effects were apparent. Usually it was not necessary to give more than 200 mg. daily. The drug was given for an average initial period of 20 days, and its administration was discontinued if no response was elicited within this period. The follow-up period ranged from 3 to 9 months. In general, 82 of the 100 depressed patients showed improvement, which was marked in 44 and moderate in 38. Patients with psychotic depression showed twice as much improvement as those with neurotic depression. All the patients with psychotic depression and most of those with neurotic depression would have required electroshock therapy if imipramine had not been used.

There was a therapeutic lag of 2 to 30 days between the institution of imipramine therapy and the onset of therapeutic response. The impression was that maintenance therapy should be continued for about 3 months after the appearance of an appreciable amount of improvement. Side-effects, such as tremor, agitation, nausea, vomiting, dizziness, and perspiration, were of minor consequence. The mode of action of imipramine was interpreted as a shift in aggressive cathecting energies of internalized object systems of control (supergo component), with a secondary reorganization of libidinal investment. The general impression was that imipramine proved to be a potent antidepressant substance, which already had resulted in a drastic decrease in the number of sessions of electroshock treatment.

The Use of Imipramine (Tofranil) for Depressive States in Open Ward Settings of a General Hospital: A Preliminary Report. R. B. Sloane, A. Habib and U. E. Batt. Canad. M. A. J. 80:540-546 (April 1) 1959 [Toronto].

Imipramine (Tofranil) was given to 8 men and 22 women, between the ages of 33 and 85 years, with symptoms of depression, most of whom had manic-depressive depressed psychosis requiring hospitalization. These 30 patients were admitted to wards of the Kingston (Ont.) General Hospital. The depression in most of these patients was characterized by subjective feelings of fatigue, weakness, slowing down, sadness, and guilt, accompanied by a loss of appetite and sleeplessness. The clinical picture ranged from severe retardation and near stupor, at one extreme, to severe agitation, at the other, through the usual intervening stages. In some patients the covert depression took the form of extreme hypochondriasis. The criterion of selection was a severity of symptoms justifying the use of electroshock therapy. Imipramine was usually given by mouth in doses of 50 mg. 4 times daily, and this remained the average dose for all patients. The upper limit of dosage was 600 mg. in one day.

Of the 30 patients, 4 recovered, 12 were much improved, 9 were improved, and 5 were unchanged; 25 patients (80%) thus obtained satisfactory results, and the mean hospital stay was 5 weeks. These results were comparable to, if not somewhat better than, those from electroshock therapy. The results of a double-blind controlled study carried out on 12 patients, 6 of whom received imipramine and 6 a placebo, showed that it was impossible to distinguish between placebo and active compound for the first 2 weeks after admission to hospital. Similarly, the improvement produced by the active drug was no better than that caused by the placebo during this time. These results suggest perhaps underestimating the value of hospital admission per se in gratifying the needs of patients with depression. Such studies need to be extended. Follow-up of the patients for 4 months after their discharge from the hospital showed that administration of imipramine probably has to be continued over a considerable period of time and remission may follow withdrawal of the drug. It is concluded that imipramine is a useful drug in the treatment of depression; further work may clarify its best usage.

Hyperinsulinism: Rare Cause of Epilepsy. D. W. Mulder and J. G. Rushton. Neurology 9:288-289 (April) 1959 [Minneapolis].

The authors direct attention to an earlier report in which Breidahl and associates reported that the condition of patients with functioning adenoma of the islet cells of the pancreas is frequently diagnosed as epileptic. Of 91 patients seen at the Mayo Clinic, 37 had what are called convulsive seizures as a clinical symptom. The recognition of seizures secondary to hyperinsulinism is of clinical importance, as hyperinsulinism due to a pancreatic adenoma may be cured surgically. Because of the frequent confusion in diagnosis between hyperinsulinism and epilepsy, some investigators have suggested that every patient with seizures should have a fasting blood sugar determination. In the experience of the authors routine determination of fasting blood sugar has not proved to be an effective aid in the recognition of hyperinsulinism.

In order to differentiate epilepsy due to hyperinsulinism from epilepsy due to other causes, the authors reviewed the records of 91 patients with hyperinsulinism previously described by Breidahl and associates. The term "hyperinsulinism" is reserved for patients in whom a hyperfunctioning tumor of the islets of Langerhans has been found. An epileptic seizure is defined as "a brief, abrupt, recurrent, paroxysmal, stereotyped cerebral storm inappropriate to the immediate situation and followed by transient impairment of cerebral function." Transient recurrent cerebral symptoms and signs were common in the 91 patients. The criteria just mentioned for recognition of an epileptic seizure were applied to these symptoms.

In 21 of the 37 patients in whom Breidahl and associates had observed convulsive seizures, the recurrent cerebral symptoms were gradual in onset, variable in manifestations, and of long (several hours to days) duration. The character of these attacks was distinctly different from an epileptic seizure. The authors, therefore, conclude that only 16 of the 91 patients had had epileptic seizures. Fifteen of the 16 patients had seizures best classified as generalized convulsions. In some the attack was typically grand mal, while in others loss of consciousness occurred with only mild tonic or clonic movements. In 9 patients prodromal symptoms of paresthesia, dazed feeling, sweating, pallor, faintness, hunger, or diplopia occurred, usually 30 minutes or more before onset of a convulsion. In 14 of 16 patients the first seizure occurred between the ages of 31 and 63 years. In 2 the first seizure occurred at ages 9 and 23 years respectively. Frequency of these seizures varied greatly. In 8 patients attacks occurred several times a week to several times a month, but the others had had only a few or single seizures.

Neurological examination and electroencephalographic study, conducted at a time when the patient did not have hypoglycemia, usually produced normal results. One patient had a positive Babinski sign and an abnormal increase in the activity of muscle stretch reflexes on the left side. In only 3 patients were electroencephalographic abnormalities noted: slight dysrhythmia in 2 and bitemporal slow waves in 1. In these 16 patients with epilepsy, the cause of hyperinsulinism was adenoma of the islet cells of the pancreas in 9 and adenocarcinoma in 7. The authors could discover no relationship between the type of pancreatic lesions and the character or frequency of the epileptic seizures.

Late Prognosis of Chlorpromazine Jaundice. A. G. Melrose and J. R. Roy. Brit. M. J. 1:818-819 (March 28) 1959 [London].

Jaundice, the best known of the complications of chlorpromazine therapy, has an incidence of about 1%. The authors cite one investigator who found that, in 55 patients hospitalized with jaundice in 1957, chlorpromazine was the cause in 5. It is believed that jaundice is caused by hypersensitivity to the drug within the liver, which may result in an increased permeability of the cholangioles. The characteristic histological picture is one of biliary stasis, with infiltration of the portal tracts by polymorphonuclear leukocytes, among which eosinophils are frequent. In most patients the period of jaundice is brief, lasting only a few weeks, but in some jaundice has been known to persist for months.

In order to ascertain whether disappearance of the jaundice is followed by complete histological and functional restoration, the authors made studies on 2 patients, a 52-year-old woman and a 48-year-old man, who had had chlorpromazine jaundice 6 months and 1 year previously. They were studied by means of liver-function tests and needle biopsy.

Neither had suffered previously from liver disorder, and no clinical stigmas of chronic liver disease were noted while they were under observation. Persistent histological changes were observed in both patients, but biliary cirrhosis was not observed. In one patient the liver function tests remained abnormal.

Chlorpromazine is of such recent introduction that enough time has not yet elapsed for the ultimate prognosis in all patients who develop jaundice to become clear. The present investigation indicates that restoration of normal liver histology or function, or both, may be long delayed. If permanent changes were to ensue, the original cholangiolytic type of lesion is of a nature that could lead to biliary cirrhosis. Literature reports are cited confirming this possibility. The authors conclude that, since the drug is potentially toxic, it should not be used without careful consideration.

PEDIATRICS

Chronic Idiopathic Hypercalcemia (Fanconi-Schlesinger Type): Treatment with Thyroxin. C. Hooft and A. Vermassen. Maandschr. kindergeneesk. 27:37-52 (Feb.) 1959 (In Dutch) [Leiden, Netherlands].

The female infant whose history is presented was born to normal parents, although the father's family included members with some defects, particularly low stature. The mother's pregnancy and delivery were normal. It was not known whether the mother had received supplementary vitamin D during her pregnancy. The infant exhibited anorexia, vomiting, and failure to thrive from birth, also constipation, retardation of both physical and mental development, marked hypotonia, a characteristic facies, small head, hypertension, and a heart murmur. The most important biochemical findings were persistent hypercalcemia, hypercholesterolemia, and subnormal renal clearances. Roentgenoscopy revealed dense transverse bands in the metaphyses of the long bones and increased density at the base of the skull. The first clinical features—anorexia, vomiting, and failure to grow normally—were definitely present before vitamin D was administered or vitaminized milk was given. The existence of increased sensitivity to vitamin D was established later.

The authors point out that hypercalcemia can develop in children not only after the administration of excessive doses of vitamin D but also in connection with certain disorders, such as hyperparathyroidism, sarcoidosis, interstitial plasma-cell pneumonia, hypophosphatasia, prolonged immobilization, and hypothyroidism, and with malignant conditions, such as leukemia, Hodgkin's disease, or sympathicoblastoma. Frequently children with these disorders are more sensitive to vitamin D than normal children. In recent years hypercalcemia without apparent cause has also been reported in the absence of the aforementioned disorders. "Idiopathic hypercalcemia in infants with failure to thrive" was described by Lightwood and Payne in Britain in 1952, and during the same year Fanconi and associates in Switzerland and Schlesinger and others in Britain described "chronic hypercalcemia, combined with osteosclerosis, hyperazotemia, subnormal growth, and malformations." It is suggested that the disorder described by Lightwood is a mild or incomplete form of the syndrome described by Fanconi and Schlesinger. The benign or incomplete form is usually reversible within a few months. The more severe form begins earlier in life, the hypercalcemia is more persistent, severe physical and mental defects exist, and death may result from renal damage or intercurrent diseases.

With regard to the case presented, the authors suggest that this type (Fanconi-Schlesinger) of idiopathic hypercalcemia results from a metabolic abnormality of endogenous vitamin-D-active substances, probably sterols. Treatment with thyroxin was followed by improvement in all the clinical, biochemical, and roentgenologic features. This favorable effect of thyroxin could not be explained by a clinically observable hypofunction of the thyroid, but it presumably resulted from the increased excretion of calcium both in the urine and in the feces. It is possible that thyroxin has a direct effect on the vitamin D activity in the serum.

A Controlled Study of Three Methods of Prophylaxis Against Streptococcal Infection in a Population of Rheumatic Children: II. Results of the First Three Years of the Study, Including Methods for Evaluating the Maintenance of Oral Prophylaxis. A. R. Feinstein, H. F. Word, J. A. Epstein and others. New England J. Med. 260:697-702 (April 2) 1959 [Boston].

Three hundred ninety-one children and adolescents, with unequivocal previous attacks of rheumatic fever, were followed at the Irvington House Prophylaxis Clinic, New York, in a special study designed to compare the effectiveness of 3 prophylactic regimens in the prevention of streptococcic infections and rheumatic recurrences. At the start of this study, a statistical method of random selection was used to divide the patients into 3 groups comparable in age, cardiac status, and duration of freedom from rheumatic activity. Each group was assigned to 1 of the 3 therapeutic agents under study: 1 Gm. of sulfadiazine given daily by mouth; 200,000 units of potassium penicillin G given daily by mouth; and injections of 1,200,000 units of benzathine penicillin G per month. The patients were examined monthly after the beginning of the study. Streptococcic infections were detected by careful bacteriological and immunological techniques (with the use of antistreptokinase and antihyaluronidase as well as antistreptolysin-O titers when necessary). Recurrences of rheumatic fever were diagnosed by means of the modified Jones criteria.

The data for the first 3 years of this study have now been completed and show the following incidence of streptococcic infections per patient year in each group: sulfadiazine, 21.1%; penicillin given by mouth, 20.7%; and penicillin given by injection, 7.3%. When the group of patients taking the drugs by mouth was divided into those who maintained good prophylaxis and those who did not, it was found that the injections were still more effective than either preparation given orally for the prevention of streptococcic infections, and that sulfadiazine had been more effective than penicillin given by mouth to patients who maintained good prophylaxis. The recurrence rate of rheumatic fever per patient year was as follows: sulfadiazine, 1.9%; penicillin tablets, 5%; and penicillin injections, 0.3%.

These data show unequivocally that injections are more effective than oral administration of either sulfadiazine or penicillin, in the dosage schedule used, for the prevention of streptococcic infections and rheumatic fever. Of the 2 agents given orally, sulfadiazine has been as good as, and possibly superior to, penicillin. This observation has many ramifications for the mass-scale rheumatic-fever prophylaxis programs now in operation. The apparent superiority of sulfadiazine is now being tested against a double dose of penicillin in a new group of patients who have been added to those in the original study.

Vasopressin-Resistant Diabetes Insipidus. S. A. Kaplan, A. M. Yuceoglu and J. Strauss. A. M. A. J. Dis. Child. 97:308-313 (March) 1959 [Chicago].

In 3 generations of a Negro family there were 8 members with vasopressin-resistant diabetes insipidus. Of the 8 patients, 4 were children (3 boys and 1 girl between the ages of 3 months and 4½ years), and 3 were adults (the mother of one of the boys and 2 of her sisters). The most remarkable feature of the disease as manifested by these patients was its extraordinary variability. Some of the patients had only polyuria and polydypsia, but in one patient there occurred, temporarily, growth retardation, hypernatremia, reduced urea clearance, and severe impairment of renal powers of base conservation. In 3 patients there was marked hyperaminoaciduria. Except for aminoaciduria and failure to concentrate maximally, renal function appeared to be normal in all the patients when this paper was written. It is worthy of note that in this family vasopressin-resistant diabetes insipidus occurred in both males and females. Reports on 120 patients with this disease were collected from the literature. The reported data support the contention that in many instances, at least, vasopressin-resistant diabetes insipidus is not transmitted by a sex-linked recessive gene but by an autosomal dominant.

THERAPEUTICS

Hemisulfur Mustard in the Palliation of Patients with Metastatic Ovarian Carcinoma. T. H. Green. Obst. & Gynec. 13:383-393 (April) 1959 [New York].

The author reports the experience accumulated between 1953 and 1958 at the Vincent Memorial Hospital in Boston in the use of hemisulfur mustard to achieve palliation and particularly control of ascites in 30 patients with disseminated ovarian carcinoma. All these patients had been given benefits of surgery and radiation therapy before the therapy with hemisulfur mustard. All of them were hospitalized during and for a few days after treatment with hemisulfur mustard. Pretreatment consisted of 0.1 Gm. of diphenylhydantoin (Dilantin) given orally 3 times daily for several days prior to the administration of hemisulfur mustard. Dilantin was continued during treatment and for several days thereafter and was given intramuscularly whenever nausea and vomiting intervened. Preparations with cerebral-stimulating effect should not be given during or immediately after hemisulfur mustard therapy. The standard course of intravenous therapy with hemisulfur mustard consisted of 3 divided doses of 200 mg. each, an interval of at least 48 hours being allowed between injections or until any signs of toxicity had subsided. It is necessary to make the injection into a large vein to avoid skin irritation and phlebitis. Occasionally the third and last injection was omitted because of the occurrence and persistence of significant symptoms of neurotoxicity. A single dosage of 300 to 350 mg. of hemisulfur mustard was used for direct intraperitoneal injection. The solution is prepared immediately before the intraperitoneal injection in exactly the same manner as for intravenous injection. Paracentesis was done with the usual small trocar, which removed about half of the ascitic fluid present.

Nineteen of the 30 patients were treated intravenously and 11 by direct intraperitoneal injection. Fifteen of the 19 patients treated intravenously and 6 of the 11 patients treated by direct intraperitoneal injection experienced significant benefit from the drug. The longest post-treatment survival to date has been 33 months among these patients; 8 patients lived, or are at present living, 6 to 12 months after treatment. Of the 9 patients who did not benefit from the drug, 3 survived for 3, 7, and 10 months, respectively, 4 died within 6 weeks of therapy, and 2 died during intravenous therapy; of the latter 2, one died of pulmonary embolism and the other in severe convulsions. Suppression of ascites was the most frequent favorable objective response, and there was complete and permanent disappearance of abdominal fluid in 62% of the patients, with significant decrease in the rate of formation in an additional 15%. In 8 patients a decrease in size of palpable abdominal or pelvic masses was observed. The intravenous administration of hemisulfur mustard seemed to produce favorable palliative effects in a somewhat greater percentage of patients than did the intraperitoneal instillations; but the single injection technique of direct intraperitoneal instillation offers many advantages to the patient in its ease and simplicity. Absence of toxic side-effects and shortened hospitalization time seem to warrant continued trial, particularly in patients who present only the problem of ascites in the absence of large masses or other manifestations of metastatic disease.

Potentiation of Biological Activities of Steroids by Carcinogenic Hydrocarbons. E. Myles Glenn, S. C. Lyster, B. J. Bowman and S. L. Richardson. Endocrinology 64:419-430 (March) 1959 [Springfield, Ill.].

Previous studies by other investigators had suggested that local implantation of certain carcinogenic hydrocarbons antagonizes or inhibits the biological response of specific target organs to androgens, estrogens, and progestational agents. It had been demonstrated that an experimental mammary fibroadenoma, refractory to steroid therapy alone, showed a marked retardation of growth when androstan-17β-ol-3-one and 3-methylcholanthrene were administered together. When administered alone, neither compound induced a marked degree of inhibition. These results led to a hypothesis that carcinogenic agents may alter the response of certain cells to steroid hormones and that systemic administration of carcinogenic hydrocarbons may produce different effects from those observed after local implantation. The experiments described here were designed to determine the influence of carcinogenic hydrocarbons on biological effects produced by androgens and adrenocortical steroids.

The authors demonstrated in experiments on rats that oral administration of 3-methylcholanthrene, 2-anthramine, benz-α-pyrene, and 7-methylbenzanthracene, all carcinogenic agents, greatly potentiated both the androgenic and the myotropic effects of 17-methyltestosterone. Noncarcinogenic hydrocarbons investigated were nearly inactive in this regard. Oral and direct administration of 3-methylcholanthrene potentiated both the glycogenic and the antiphlogistic properties of hydrocortisone. Inactive hydrocarbons, anthracene and phenanthrene, failed to induce this type of phenomenon. Both in vivo and in vitro studies indicated that the ability of carcinogenic hydrocarbons to potentiate biological effects of steroids is due to a direct effect of the carcinogenic agent at the cellular level and not to a decreased rate of steroid metabolism by the liver.

Glycine in Hypochromic Microcytic Anemia. A. Y. Kim, W. A. Beck, C. H. Kim and H. S. Portogallo. Northwest Med. 58:383-388 (March) 1959 [Seattle].

This report is based on observations made with Glytinic, a hematinic agent supplemented with glycine and containing ferrous gluconate, B vitamins, and trace elements, in the treatment of 60 patients with hypochromic microcytic anemia. There were 2 groups of patients, those who did not respond to the usual iron therapy and those who demonstrated an intolerance to iron therapy. Thirty of the patients who did not respond to iron therapy were patients in whom anemia developed as a result of long-standing low-protein intake. Twenty of these patients were given 100 mg. of iron as ferrous gluconate in a daily dose for 90 days and 10 were given 333 mg. of ferrous sulfate for 60 days daily, but no hematological response was noted. When Glytinic was administered, however, the hematological response was good. The remaining 30 patients who had demonstrated an intolerance to iron therapy or ferrous sulfate all responded well to the administration of the glycine-supplemented hematinic. Glycine was felt to be of value as an amino acid concerned with hemoglobin synthesis or as an expedient source of nitrogen for the production of other amino acids required for hemoglobin synthesis. Only 5 out of 656 patients who were tested over a 4-year period by the authors demonstrated mild gastrointestinal disturbance, which shows that a glycine-supplemented hematinic is well tolerated.

PATHOLOGY

Alcohol as a Factor in Medico-Legal Sudden Deaths. C. Duncan. M. J. Australia 1:322-323 (March 7) 1959 [Sydney].

It has been pointed out that, while it is illegal to take without consent blood from a live person for the purpose of alcohol estimation, there is no fear of a charge of assault when the blood is taken from the dead body at an autopsy. There are satisfactory methods for estimating the postmortem blood alcohol levels, and the results are reliable if the blood is taken from a peripheral source, but are open to errors if it is taken from the heart, the chest, or the abdominal cavities. The author says that in Hobart, Tasmania, the value of blood alcohol tests in connection with the coroner's work has been realized for a long time, but until fairly recently facilities for performing the estimations were lacking. Now they are carried out in the government analyst's department.

Whenever possible, blood is withdrawn by cutting through a femoral vein, and several milliliters can usually be obtained. Occasionally, in subjects with great blood loss, the femoral vessels are empty, and it is necessary to depend on the cerebral vessels. Urine also is collected, if the femoral vein site is unsatisfactory, or if there are unusual circumstances about the death. The blood or urine is delivered immediately to the analyst, who adds fluoride as a preservative if the test is not made until later. The analyst reports the alcohol content of the blood in milligrams per 100 ml. of blood, works out the total amount of absolute alcohol present in the body on the basis of the deceased's weight, and then gives the amount of whisky and beer which is equivalent to the calculated amount of alcohol present. The test is not used in all deaths but in murder, manslaughter, and some traffic accidents and in cases in which alcohol is suspected as a causative factor in the death. The findings in a consecutive series of fatal traffic accidents over a period of 3½ years are given in a table, and several cases in which the test proved important are described.

The Technic of Nuclear Sexing. D. J. B. Ashley. Am. J. Clin. Path. 31:230-237 (March) 1959 [Baltimore].

The technique of nuclear sexing is now a well-established research method, and its wide range of applications leads to an increasing flow of requests to the pathologist for this examination. It is the purpose of this paper to describe the methods generally used for this test, and to demonstrate that it is not an esoteric research method to be used only by special departments but is within the scope of the general pathologist. Cells from practically any tissue of the body may be used for "sexing," but it is usually most convenient to use material which may be obtained with minimal discomfort to the patient. The cells of the squamous epithelium of the skin in man are particularly suitable and can be readily obtained either as a formal skin biopsy or by scraping cells from the inside of the mouth.

The sex chromatin body is a mass of heterochromatin, 0.7 by 1.2 μ in mean dimensions. It lies in the nucleoplasm of the cell and is most often located near the nuclear membrane. It stains deeply with the specific nuclear stains, and a deep red-violet by the Feulgen technique, and appears as a small body that is much darker than the remainder of the nucleus. In the usual position, adjacent to the nuclear membrane, it has a planoconvex form with the plane surface closely applied to the nuclear membrane, but if it lies free in the nucleoplasm, it assumes a circular shape. Sex chromatin can be identified in 80 to 90% of the cells of the normal female. Masses of chromatin, morphologically similar to those seen in the female, may be seen in a small proportion of the cells of the normal male. These bodies are not the same as those found in the female, but consist of irregular aggregations of nuclear material. The frequency of these irregular chromatin masses is always less than 10% in the cell nuclei of the male. When the strictest criteria are used, the frequency of identified sex chromatin in the cells of the female is less than 80 to 90%.

An alternative method of diagnosis of genetic sex by means of the cells of the peripheral blood was described in 1954 by Davidson and Smith. These 2 workers demonstrated that a small proportion of the polymorphonuclear leukocytes in normal women had a small projection approximately the same size as the sex chromatin body observed in the somatic cells. This projection, which they termed the "drumstick," was present in at least 6 of every 500 cells in the female, but true drumsticks were never seen in the male. The technique of leukocyte sexing is simple. Films are made from the peripheral blood, preferably on cover slips, and are stained by the routine methods for blood films—Leishman's, Jenner-Giemsa's, or Wright's stain. If 6 or more drumsticks are observed in the examination of 500 polymorphonuclear leukocytes, the patient is regarded as female; if less than 6 bodies resembling drumsticks are observed, the patient is regarded as male. The drumstick is a spherical body, about 1μ in diameter, and is attached to the side of the lobulated nucleus by a thin stalk. Care must be exercised to exclude from consideration small sessile appendages attached to the body of the nucleus by a thick stalk, racquet-shaped bodies that often manifest central vacuolation, and small lobes at the extremities of the nucleus that may be observed in either sex. Many investigators have confirmed the findings of Davidson and Smith, but in a few instances discrepancies have been noted between the results obtained by the leukocyte method and those obtained by the use of somatic tissue cells. Stress is placed on the necessity for experience in the tests and the use of control material.

Behavior of Certain Enzymatic Activities in the Course of Ischemic Syndromes of Obliterating Arteriopathy of Lower Extremities: Aspartic Transaminase, Alanine-Ketoglutaric Transaminase and Phosphoglucomutase. A. Di Simone and G. Ferrante. Minerva chir. 14:123-127 (Feb. 15) 1959 (In Italian) [Turin, Italy].

Serum aspartic transaminase, alanine-ketoglutaric transaminase, and phosphoglucomutase levels were studied in 20 patients, aged between 12 and 73 years, with acute and chronic arterial disease of the lower extremities. Atherosclerosis was present in 18 patients, thromboangiitis obliterans in 6, arteriopathy of diabetic origin in 3, acute thrombosis in 1, postembolic arteriopathy in 1, and arterial lesion probably related to virus in 1. Serum aspartic transaminase and alanine-ketoglutaric transaminase levels rose proportionally with the severity of the disease in patients with arteriopathy obliterans. The values remained within the physiological limits in instances of arteriopathy not associated with ulcerative or gangrenous lesions, they were high in the presence of ulceration or gangrenous states. Very high values of serum aspartic transaminase and alanine-ketoglutaric transaminase activities were observed in patients who had an acute onset of ischemic disorder not necessarily related to a severe necrosis. Of the patients with diabetic arteriopathy. values did not change in 2 with severe arterial lesions but changed in 1 with average severe form of the disease.

The serum phosphoglucomutase level increased, but not as markedly as the levels of the 2 transaminases, in patients who had acute or chronic ischemic disorders associated with extensive tissue degeneration. No changes in the transaminase activity took place in instances of diabetic arteriopathy. However, the values of enzymatic activity were high in 2 patients before amputation of a leg affected by gangrene, but they returned to normal after completed cicatrization. This investigation suggests that there exists a pathological nexus between the variation of serum enzymatic activities and certain types of obliterating arteriopathy, particularly those related to muscular necrosis.

Transformation of a Normal into an Active Breast with Milk Secretion in the Course of Malignant Tumors and After Ovariectomy. G. Piacentini. Policlinico (sez. prat.) 66:249-256 (Feb. 23) 1959 (In Italian) [Rome].

Reactivation of a normal and quiescent mammary gland, accompanied by milk secretion from the breast on mild compression, and hyperpigmentation of the areola and nipple of the breast were observed in 2 women in the course of an advanced phase of malignant neoplastic disease. A nodule on the right side of the inguinal region appeared in one woman at the age of 37 years when she reached the menopause. She had begun to menstruate at the age of 13 and had had 5 normal deliveries. A course of roentgenotherapy had been started 10 months after the appearance of the nodule, at the time that it had started to grow. The nodule enlarged into an ulcerating tumor and was diagnosed as a polymorphous sarcoma. Pulmonary and intra-abdominal metastases appeared 6 months after the completion of the roentgenotherapy. At this stage profuse milk secretion was observed on mild compression of the breast. This anomaly persisted until the patient's death.

A small painful nodule with retraction of the nipple developed in the other woman at the age of 30. She had had 2 children and normal menstruation. A radical mastectomy for carcinoma of the breast and metastases in the axillary lymph nodes was performed a month later. Ovariectomy was done 4 months after the mastectomy. Widespread skeletal metastases were observed a month after the ovariectomy. Carcinomatous metastases were simultaneously revealed in the region of the resected breast. The remaining mammary gland was reactivated and continued to secrete milk until the patient's death.

The author believes that the pituitary body was either the main factor or was subsequently involved in the process of the neoplastic disease in the first patient who had a precocious menopause. In the second patient rapid development of metastases in the bones and skin and lymph nodes, with reactivation of a quiescent mammary gland after ovariectomy, supports the hypothesis of a correlation between malignant neoplastic disease and the activity of glands of internal secretion.

Renal Lesions in Scleroderma: Clinical and Pathological Features. J. D. Tange. Australasian Ann. Med. 8:27-34 (Feb.) 1959 [Sydney, Australia].

Scleroderma is a generalized disease, apparently primarily affecting the small vessels. Since it produces such characteristic and striking changes in the skin, attention was at first attracted to this; however, the presence and importance of visceral, and especially of renal, involvement have now become more widely recognized. The author cites previous investigators, who emphasized the nature and consequences of renal lesions, and then describes observations on 3 patients, who were women ranging in age from 36 to 69 years. The disease lasted 2 years in one of these women and 1 year in each of the others. The terminal phases lasted 6, 12, and 2 weeks, respectively, and were heralded by rising blood pressure and albuminuria. In 2 cases there was papilledema together with retinal hemorrhages and exudates. In the third there was no record of ophthalmoscopic examination, but the course was such that these changes were likely to have been present. Two of the 3 patients received adrenal cortical steroids. In both the blood pressure had already risen before treatment was instituted, but the progress of the disease seemed to be accelerated after the steroid administration.

The significant renal lesion in scleroderma is a mucoid or loose fibrous swelling of the walls of the intralobular arteries, involving the entire wall or the intima alone without inflammatory cell reaction; the lumen is substantially narrowed or obliterated. Interference with cortical blood flow leads to necrosis and thrombosis of the afferent arterioles and focal infarcts of the cortex. Clinically, these changes are mirrored by rapidly progressive renal failure or by severe hypertension or both. The clinical features and the renal lesions closely resemble those described in malignant or rapidly progressive hypertension. Corticosteroids accelerate the progress of the hypertension or may even determine its appearance. Thickening of the basement membranes of the glomerular capillaries is found independently of these arterial lesions. The histories of patients showing this glomerular change suggest that it is probably related clinically to the occurrence of a trace of albumin in the urine, and that the appearance of albuminuria does not necessarily presage the onset of severe hypertension and renal failure. The author suggests that the occurrence of renal failure in 5 of 31 patients who died of scleroderma and the increasing number of reports in the literature permit an estimate of the incidence of these complications.

Sex Chromatin in Cultured Normal and Cancerous Human Tissues. C. P. Miles. Cancer 12:299-305 (March-April) 1959 [Philadelphia].

Cells from 21 tumors obtained from 11 women and 10 men were examined for sex chromatin after the tissues had been cultured in vitro. With 2 exceptions, the female tissues showed sex chromatin in high percentages, while the male tissues did not. There was no significant difference with regard to sex chromatin between normal and cancerous outgrowths from primary explants. It is probable that not all nuclei from female tissues contain sex chromatin clumps. Either the sex clump cannot occur at any point on the nuclear membrane or else the nucleus is not oriented at random with the culture substrate. It may be concluded from this study that at least some malignant tumors from women continue to show sex chromatin in in vitro culture. It is doubtless also a safe inference that these cells possess the sex clumps in vivo, however difficult the demonstration of sex chromatin may be in tissue sections of tumors. The finding that sex chromatin does persist, at least in primary explants, may have experimental as well as clinical value.

RADIOLOGY

Lymphangioma of the Duodenum. J. G. Davis, H. Peck and B. L. Gray. Am. J. Roentgenol. 81:613-615 (April) 1959 [Springfield, Ill.].

The authors present the case of a 65-year-old man who complained of crampy right upper quadrant abdominal pain of 9 months' duration, usually occurring after meals and nocturnally, aggravated by spicy foods, and relieved by eating and drinking milk. He denied nausea, vomiting, melena, jaundice, change in bowel habits, or weight loss. Upper gastrointestinal roentgen-ray examinations revealed a small hiatal hernia and a deformed duodenal cap. In the 4th portion of the duodenum, a circumscribed oval filling defect with intact overlying mucosa was demonstrated. Surgical intervention revealed that the deformity of the duodenal cap apparently was the result of adhesions from a chronically infected gallbladder containing nonopaque stones. In the superior wall of the 4th portion of the duodenum near the ligament of Treitz, a soft, boggy, slightly irregular submucosal mass was found, measuring approximately 3 cm. in its greatest dimension. This appeared grossly benign, and frozen section microscopically revealed a lymphangioma.

Only 10 cases of lymphangioma of the gastrointestinal tract have been described in the English literature. There have been no previous reports of lymphangioma in the duodenum. Lymphangioma is one of the least frequent of the benign tumors of the small intestine. It is thought to arise from the lymphatic plexus in the submucosa into which the lacteals of the villi empty. Many believe the tumor develops from misplaced embryonic tissue, but evidence to support this is lacking. A more plausible cause seems to be stasis and back pressure brought about by blockage from the mesenteric lymph nodes. Tumors of the small intestine may or may not be symptomatic. If symptoms are present, they can be of 3 types: (1) obstructive; (2) bleeding; and (3) symptoms arising from local irritability, such as ulcer-like pain, vague signs of indigestion, nausea, belching, and occasionally vomiting. Intussusception may be found. The roentgenologic aspects of lymphangioma are those of a submucosal intramural tumor, usually with overlying intact mucosa.

Six Primary Adenocarcinomas of the Colon Occurring Simultaneously: Report of a Case. W. Molnar. Am. J. Roentgenol. 81:678-682 (April) 1959 [Springfield, Ill.].

Studies based on large numbers of collected cases show that the average incidence rate of multiple malignant lesions of the colon is between 3 and 4%. Old age apparently is not a factor in the occurrence of multiple lesions, since the mean age for such patients is less than for patients with single lesions. Adenomatous polyps are believed by many authors to be precancerous lesions because of the higher incidence of benign polyps associated with malignancy. Predisposition or "inherent susceptibility" to cancer seems to be the most important single factor in the production of multiple malignant lesions of the colon. The case presented was that of a 75-year-old diabetic woman, who had had adenocarcinoma of the endometrium in 1944. This lesion had been treated by irradiation, followed by hysterectomy. In 1953 the patient complained of having had midabdominal pain since the preceding month, associated with nausea and vomiting during the last 3 days. A supine roentgenogram of the abdomen on the day of admission showed markedly distended ileal loops as well as distention of the proximal colon. After the abdomen had been decompressed with the aid of a Miller-Abbott tube, an examination with the use of barium showed a polypoid mass involving a 5-cm.-long segment in the midportion of the elongated sigmoid. There was another small mass in the region of the splenic flexure. A 7-cm. segment of the hepatic flexure narrowed down to an irregularly outlined, rigid channel, causing delay in filling of the ascending colon with barium. Spot roentgenograms taken of these 3 lesions showed the details of the tumors. The 14-by-17-in. roentgenograms of the filled colon demonstrated another rounded mass, 4 cm. in diameter, at the medial aspect of the cecum, which was believed to represent lipoma of the ileocecal valve. The advanced lesions in the hepatic flexure and in the sigmoid were obscured because of the tortuosity of these segments. At follow-up examination by air-contrast study, 2 additional polypoid lesions were visualized, one in the proximal sigmoid and another in the region of the midtransverse colon.

At laparotomy only 4 lesions were palpable, besides the lipoma in the ileocecal region. Although a total colectomy was contemplated, the procedure had to be terminated after the resection of all the colon proximal to the midsigmoid. The patient died on the same day. The distal half of the sigmoid and the rectum were examined at autopsy. The lesions varied in size. The most advanced carcinoma in the hepatic flexure was the most proximally located, implicating cellular seeding as a possible explanation for the development of the smaller-sized and less-advanced lesions in the left side of the colon. There was no evidence of concomitant adenomatous polyps on the removed specimen. No other similar case report could be found in the English literature.

PUBLIC HEALTH

Two Epidemics of Injection Diseases. H. C. Zanen. Nederl. tijdschr. geneesk. 103:271-276 (Feb. 7) 1959 (In Dutch) [Amsterdam].

In 1951 hepatitis was declared to be a notifiable disease in the Netherlands, and from 1951 to 1957 a total of 4,276 cases of infectious hepatitis and 45 cases of serum hepatitis were reported in Amsterdam. Every patient with hepatitis was subjected to a thorough epidemiologic investigation with regard to blood transfusions, skin tests, or any type of injection (including those performed by a dentist) during the 6 months preceding the onset of their hepatitis. The patient was questioned also about the occurrence of other cases of jaundice in his environment. These inquiries revealed that, in 419 of the patients with hepatitis reported, one of the aforementioned interventions had been carried out during the 6-month period; no other cases of hepatitis had occurred in the environment, so that a diagnosis of serum hepatitis seemed possible in about 10% instead of in only 1% of the patients. In classifying the patients according to age, it became apparent that in those more than 40 years old about 50% could have had serum hepatitis. Further analysis of the types of treatment received and of the places in which the treatment had been carried out revealed that a large number of hepatitis patients had received treatment at one particular outpatient clinic. It was ascertained also that, during periods when work was pressing, the nursing staff of this clinic changed the needle but not the syringe, when drawing blood for the determination of the erythrocyte sedimentation rate. When a sterile needle and syringe were used for every patient, no new cases of hepatitis developed.

In the course of immunizations of school children against diphtheria, inflammatory reactions were found to be more frequent than usual. In one school abscesses developed in 6 of 77 children who had been inoculated. Hemolytic streptococci, group A, type 12/27/44, were isolated from 3 of these abscesses. Scarlet fever was diagnosed in one child one day after the immunization. The abscesses were attributed to accidental contamination of a common filling-needle. It is pointed out that the use of a common filling-needle for a number of injections constitutes a potential danger of infection and is to be condemned.

How Did They Die? A Study on the Occupational Mortality in Three Swedish Professions. E. Ask-Upmark. Acta med. scandinav. 163:89-104 (no. 2) 1959 (In English) [Stockholm].

This study was originally started to ascertain the cause of death in university professors, because 2 famous professors in the linguistic sciences had died of malignant glioma of the brain, and a noted pathologist is said to have ascribed the preponderance of gliomas in males to their cerebral activities. In an earlier study the author had been able to demonstrate the predilection of gliomas for the more recently developed parts of the hemisphere, the regions of human achievement. Yet the strain on the vascular system of the brain might be presumed to be considerable in a mental worker, and the question had to be answered whether vascular lesions were more frequent in the brains of scholars. The author compared the mortality in 382 Swedish university men, 508 Swedish printing workers, 741 Swedish street-car employees, and 700 American physicians. (Data on the last group were obtained from The Journal). All were males, and no case of death under 30 was included. The records for the 4 groups covered different periods: those for the Swedish university men, the years from 1900 to 1957; for the printers, 1925 to 1955 (with some exceptions); the street-car men, 1944 to 1956; and the American physicians, the year 1957.

The Swedish university men did not present any increased incidence of cerebrovascular lesions or of intracranial neoplasms. The incidence of tuberculosis and suicides was rather on the low side. The incidence of pulmonary carcinoma was strikingly low (2 cases). Otherwise the causes of death in the professors were about the same as those in the average population. The printers died, on an average, 10 years younger than the university men; yet malignant tumors accounted for a large percentage of their deaths. Bronchial carcinoma was particularly frequent during the last 9 years, accounting for 15 of 267 deaths. Tuberculosis also accounted for a strikingly large number of deaths among the printers, but vascular lesions of the brain were less frequent than in other groups. Street-car men at the time of death were, on an average, 7 years younger than the university men but 3 years older than the printers. Malignant tumors were just as common in this group as in the group of printing workers, although the proportion of bronchial carcinomas was less pronounced. A striking feature, as yet unexplainable, was the high incidence of intracranial tumors, and suicides were rather more common than in the average population. The American physicians served as a control group. Their average span of life approached that of the Swedish university men. The most striking feature was the high incidence of cardiovascular deaths, amounting to more than 50% of all deaths, 3 out of 4 cardiac deaths being due to coronary lesions.

The author concludes that the Swedish university men died of essentially the same causes as did men in the general population. There was not the slightest evidence that the work of the scholar would predispose to the development of cerebral disease. The average age of the university men exceeded that of the more manual workers, and bronchial carcinoma as a cause of death was strikingly rare.

Profile of American Families, 1940-57. W. F. Pratt. Pub. Health Rep. 74:189-194 (March) 1959 [Washington, D. C.].

The author shows that marked changes are occurring in the patterns of American family life, many of which have proceeded more rapidly since World War II. The number of families in the United States has increased. More than three-fourths of the decline in the proportion of the population "never married," since 1890, occurred between 1940 and 1957. In this period the proportion of men currently married increased from 59.7 to 67.3%, and of women from 59.5 to 66.4%. The number of families increased 35.1% between 1940 and 1957. Several factors have contributed to this increase in families: 1. More couples survive to celebrate their golden wedding anniversary. 2. The proportion of remarried persons has increased. 3. The proportion of persons remaining single has declined. 4. Better economic conditions have contributed to the increase of families by decreasing the "doubling-up" in households.

In commenting on fertility rates, the author says that parents today apparently want, or can afford, to care for more children. In 1956 the fertility rate reached 120.8 infants born alive per 1,000 women, 15 to 44 years of age, which is in sharp contrast to the 1940 rate of 79.9 and is in excess of the 1947 rate of 113.3, the year of the "baby boom." Most important for trends in family size is that the increase in fertility rates in recent years has been due to increasing rates of third and higher order births, which have continued to rise since 1950. However, despite the marked increase in fertility and children born, the average size of families has increased but little and only in the last few years.

Changes in the household and family situation of persons over 65 years of age have been small, but in the direction of increasing isolation from kinsfolk. Between 1950 and 1957 the proportion of persons over 65 who were classified as unrelated individuals or inmates of institutions increased from 23.5 to 24.8%, or by 3,645,000 persons.

The social and economic conditions of families have generally improved throughout the period 1940-1957. This has been largely due to the increasing number of families with more than one earner and especially to the increase of women in the labor force. Despite the increasing number of dependent children in families, the participation of married women in the labor force has increased. On the basis of available data, it is extremely difficult to assess the trend in family stability, but the increasing proportion of remarried persons and the increasing proportion of divorced persons suggest a growing problem of family instability. While many of the trends in American family life, especially since World War II, may be regarded as encouraging, sight must not be lost of the fact that many social problems thought to be closely related to family life have been increasing. These are juvenile delinquency, mental illness, illegitimacy, and living conditions and productive opportunities for elder citizens. A basic step in understanding these problems and effecting preventive techniques lies in a more detailed study of the family as the unit of social, mental, and physical health. The author cites the need of more centralized registration as well as more intensive study of health conditions and of the functions of the family in rehabilitation and in preventing and treating illness.

BOOK REVIEWS

Textbook of Surgery. Edited by H. Fred Moseley, M.A., D.M., M.Ch., Assistant Professor of Surgery, McGill University, Montreal, Canada. Third edition. Cloth. $17. Pp. 1336, with 846 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1959.

This edition continues to be one of the leading single-volume references in the field of surgery for the medical student, surgical intern, and resident. It contains the work of 40 contributors, some of whom are new and others of whom have drastically revised and improved the sections involving their field of interest. This textbook is copiously illustrated, excellent use being made of the Ciba collection. Many of the plates are in color. The type is clear and easily readable. The chapters which have been added, particularly the section on pediatric surgery, are a great asset to this edition. Other excellent presentations to be noted are the sections on fractures, cardiovascular surgery, the evolution of modern surgery, the diagnosis of the acute abdomen, and pancreatic disease.

If any constructive criticism might be offered for future editions, it would be in the sections on thyroid carcinoma, parathyroid disease, and the surgical management of duodenal ulcers. Much recent experimental work and commentary in these areas has been excluded from this textbook which might have clarified the presentation in these fields. The sections on peripheral vascular diseases are extremely well done, except that on the treatment of peripheral embolization. Immediate operation appears to produce better results as regards limb salvage and usefulness than any conservative measures. The student of surgery is interested in comparative statistics, particularly as pertains to the surgical treatment of carcinoma in varied areas. This edition might benefit by more attention to this item in the future. Despite these minor shortcomings, the book is worthy of the attention of medical students, interns, and residents in the field of surgery.

Bacteriophages. By Mark H. Adams. With Chapters by E. S. Anderson, J. S. Gots, F. Jacob and E.-L. Wollman. Cloth. $15. Pp. 592, with 17 illustrations, electron micrographs by E. Kellenberger, Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1959.

This book should be welcomed by all whose attempts to keep pace with the rapid developments in modern bacteriophage research have been frustrated by an overwhelming array of special articles and reviews. This is the first attempt in over 30 years to bring the knowledge of bacterial viruses under one cover. The book was essentially completed by the author before his untimely death. Its eventual posthumous publication was made possible through the cooperation of a number of specialists who helped to edit the completed chapters and finish the uncompleted ones. The result is a well-written book. With remarkable ease of presentation and readability, a complete perspective of the field is unfolded. The bacterial viruses are first considered as organisms; their chemical, morphologic, and antigenic properties and how they are affected by physical and chemical agents is described. Then follows a detailed account of various phenomena which result from the interaction of the bacteriophages with their hosts. Phage genetics, lysogeny, colicins, phage typing, and taxonomy are also considered. A glossary and valuable appendix covering methods and techniques complete the volume. This book should be of special interest to all students of virology, bacteriology, biochemistry, and genetics. Those who are involved in any phase of virus research should find it a welcome addition to their bookshelves.

Klinische Methoden der Blutgerinnungsanalyse. Von Prof. Dr. J. Jürgens und Doz. Dr. F. K. Beller. Mit einem Geleitwort von Prof. Dr. M. Gänsslen, Direktor der II. Medizinischen Universitätsklinik Frankfurt am Main. Plastic. 56 marks; $13.35. Pp. 391, with 104 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave,. New York 16], 1959.

The advances in the understanding of the physiology and pathology of blood coagulation have been bewilderingly rapid in recent years. Even the experts in the field have difficulty keeping pace. The others, including scientists in related fields and clinicians, have all but given up hope of being able to maintain an understanding of and a critical point of view in relation to these important developments. This is probably the reason for the large number of monographs on this subject written from various points of view. The present contribution is an attempt by two distinguished German investigators to give a comprehensive and critical review of the present-day knowledge of this subject.

As indicated in the title, the emphasis is on techniques. The first chapter deals with the modern concepts of the physiology of blood clotting, which consists of an initial prophase and four phases. During the prophase, active thromboplastin is formed from platelets and plasma factors. Conversion of prothrombin to thrombin, of fibrinogen to fibrin,

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

clot retraction, and fibrinolysis take place in the four phases of coagulation. The role of inhibitors in all but the third phase is described. The presentation of this complex part of the subject is up to date with relatively few defects. For example, on the basis of a paper published in 1949, Quick is quoted as designating the factor VII principle as a special inactive precursor of prothrombin. This point of view was given up by Quick several years ago.

The second chapter deals with disorders of coagulation. Several practical and important topics including changes of coagulation in various diseases, the use of the artificial kidney, problems met in the use of extracorporeal circulation, diagnosis of impending thrombosis, and anticoagulant therapy are discussed. The equipment of the coagulation laboratory is presented in a brief chapter. Then follow 12 chapters on technique including quantitative and qualitative examination of platelets; plasma factors involved in the prophase and first phase of coagulation; tests for determination of fibrinogen, the fibrinolytic system, coagulation time, and clot retraction; the mathematics of calculation of clotting factors; the steps involved in the elucidation of the causes and in the differential diagnosis in a patient with a hemorrhagic disorder; tests for heparin; and the preparation of the many delicate reagents used in coagulation studies. The bibliographic references are as complete as one would wish. The paper, binding, print, and illustrations are of high quality. The book can be recommended as a most useful source of information to clinicians, pathologists, investigators, and students of blood coagulation.

Diseases of Women. By ten teachers under direction of Frederick W. Roques, C.B.E., M.D., M.Chir. Edited by Frederick W. Roques, John Beattie, and Joseph Wrigley. Tenth edition. Cloth. $8. Pp. 556, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-43 Maddox St., London, W. 1, England, 1959.

The first edition of this book appeared 40 years ago and was written primarily as a textbook for use by medical students. The present editors have brought the book up to date by including data on vaginal cytology and by rewriting the sections on genital prolapse, tuberculous salpingitis, and gynecologic operations. This edition contains 75 pages more than the previous one. In general, the arrangement of the subjects is the same as before. Because the 10 contributors are experienced gynecologists and teachers the book contains a large amount of practical and useful information. It is well written and abundantly illustrated. It is questionable whether the 48 pages devoted to gynecologic operations should have been included in a book written primarily for medical students. Among the operations described and illustrated are such unusual operations as radical excision of the vulva, construction of an artificial vagina, enlargement of the vaginal introitus, the "sling" operation, and radical abdominal hysterectomy for carcinoma of the cervix. In spite of this minor criticism undoubtedly the book will continue to be popular.

The Physiopathology of Cancer. By 32 authors. Edited by Freddy Homburger, M.D. [First edition edited by Freddy Homburger and William H. Fishman.] Foreword by Joseph C. Aub, M.D., Sc.D. Second edition. Cloth. $33. Pp. 1180, with 189 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1959.

The four parts of this book deal with the biology of cancer, the chemistry and physics of cancer, clinical investigations into the etiology and endocrinology of cancer, and some practical applications of the foregoing in chemotherapy, diagnostic exfoliative cytology, and radiation therapy. The amount of information presented is overwhelming, and the book is not one to be read continuously from cover to cover. Perhaps its size is a good omen, presaging a breakthrough in cancer research, for it reminds one of the large volumes on glycosuria and carbohydrate metabolism that reflected the unhappy state of diabetes research just before the discovery of insulin in 1922.

A few criticisms are offered as suggestions to prospective authors of similar works and to the present authors in case future editions are contemplated. The statistical formulas in this book are not always set up in a way that enables the reader to tell whether a succession of two or more letters denotes the product of two or more quantities or simply represents the abbreviation for a single quantity. The index is rendered tricky by overclassification, so that one finds "plutonium" and "thorium," for example, not under P and T but under C for "carcinogens." Neither the index nor the table of contents helps the reader to locate discussions of such important questions as the existence of precancerous lesions or the alleged carcinogenic action of smegma. These faults, together with some unevenness of space-allocation for various subjects, detract but slightly from an otherwise splendid piece of work. Copious bibliographies follow each chapter. The book should be valuable to everyone engaged in research on the rapidly developing subject of cancer.

Progressive Exercise Therapy in Rehabilitation and Physical Education. By John H. C. Colson, F.C.S.P., M.S.R.G., M.A.O.T., Principal, School of Remedial Gymnastics and Recreational Therapy, and Director of Rehabilitation, Pinderfields Hospital, Wakefield. With foreword by J. M. P. Clark, M.B.E., M.B., Ch.B. Cloth. $4.50. Pp. 184, with 174 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; John Wright & Sons, Ltd., 42-44 Triangle West, Bristol 8, England, 1958.

Except for brief explanations of the conditions for which they are prescribed this book consists almost entirely of exercise directions and diagrams.

The volume is divided into three parts dealing with (1) progressive exercises for the various body parts, (2) specific exercises for use in certain postoperative conditions, and (3) general exercises for supplementary conditioning. In the first section, the progression is developed by classifying the exercises as elementary, intermediate, and advanced with gradations within each of these groups. Exercises for specific therapy are grouped in primary and secondary categories and also in terms of their use at various periods during recovery and rehabilitation. General exercises include warming up exercises, which may be done to music, and "circuit training" routines, which employ a set of consecutively numbered exercises which each performer repeats according to his ability. Exercise gradations are developed with consideration for both strength and mobility. While the progressions apparently are carefully developed on the basis of wide clinical experience, they in no way obviate the need for prudent individual prescription of the exercises. No system of gradation can take the place of painstaking attention to the individual needs of the patient on the part of the physician and physical therapist. Used in this way the progressions should be helpful in planning treatment and rehabilitation programs.

The Investigation of the Relative Function of the Right and Left Lung by Broncho-Spirometry: Technique, Physiology and Application. By Frank Bergan, M.D. Paper. $4.50. Pp. 145, with 85 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1957.

This excellent monograph describing the technique, physiology, and applications of bronchospirometry is by the assistant surgeon in charge of the University Institute for Respiratory Physiology in Oslo, Norway. In many situations, particularly where an operation is contemplated or has been performed, it is important to know the respiratory function of each lung. Bronchospirometry provides this information, but the technique of intubing each main bronchus and of getting an accurate and reliable test is so difficult that the procedure is rarely used and more rarely used well. Realizing this, the author has described his technique in detail, listing the difficulties he has encountered and the manner in which he has overcome them. Among other things, he has devised a bronchospirometer tube which is well tolerated and which can be easily constructed. The remainder of the book is devoted to a report of studies on the effect of position on the function of each lung and to the application of the method in preoperative and postoperative studies. The volume is an important contribution, particularly because of the detailed description of the technique of this valuable but difficult procedure.

Pathogenesis and Treatment of Parkinsonism: Sixth Annual Scientific Meeting of the Houston Neurological Society, Texas Medical Center, Houston, Texas. Compiled and edited by William S. Fields, Professor and Head, Division of Neurology, Baylor University College of Medicine, Houston. Cloth. $10.75. Pp. 372, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

Such a comprehensive review of the most recent concepts of hyperkinetic disorders has been eagerly awaited by those interested in these diseases. This volume resulted from the symposium held by the Houston Neurological Society in March, 1958. The material is so presented as to delineate clearly what is known about these disorders, while at the same time the reader is made aware of the general misconceptions and dilemmas that persist in regard to Parkinsonism and related entities. Problems of epidemiology and basic experimental studies relating to the genesis of tremor and other hyperkinetic phenomena are discussed. A section on the pathology of Parkinsonism points out the problems involved and the heterogeneous histological changes that may be found. Information on the inclusion bodies previously described by Lewy in these diseases is also included. A historical review of the surgical attempts to alleviate the various abnormal movements and alterations in tone associated with these diseases provides additional color. The advantages of surgical procedures such as cortical excisions, pallidoansotomy, chemopallidectomy and thalamectomy, anterior choroidal artery occlusion, and the more recent ultrasonic irradiation techniques are described in the closing chapters. The controversy about the role of the corticospinal tract in tremor is aired in this volume and should prove exciting to the reader. This volume should prove valuable to all who are interested in the hyperkinetic disorders.

VA Prospectus: Research in Aging. Cloth. $1.50. Pp. 125, with 48 illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1959.

The brevity and high quality of this monograph should make it appeal to more readers than some of the recent more lengthy publications on similar subjects. This is a collection of the papers and comments of the participants in a conference called by the Veterans Administration Advisory Committee for Problems of Aging, May 16, 1958. Since diseases associated with aging account for a rapidly increasing proportion of the Veterans Administration hospital population, essential elements of current medical knowledge and thoughts concerning aging are presented in order to focus better the future research projects on aging within the Veterans Administration. Research on the aging of the molecules is discussed by Isidore Gersh and research on aging of the cells by Robert J. Boucek.

The volume goes on to a discussion of research on the organs by James E. Birren, research on persons by Charles F. Geschickter, and research on groups by Jack Weinberg. This list of contributors attests to the high quality of the monograph.

Surgery of the Sympathetic Nervous System. By Professor Sir James Paterson Ross, K.C.V.O., LL.D., M.S., Director of Surgical Professorial Unit, St. Bartholomew's Hospital, London. Third edition. Cloth. $8. Pp. 170, with 51 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Baillière, Tindall & Cox, 7 & 8 Henrietta St., Covent Garden, London, W. C. 2, England, 1958.

In this concise, readable book the drawings are simple and pertinent to the text. The author has had over 30 years' experience with surgery of the sympathetic nervous system and is well aware of its limitations. The section on anatomy and physiology is brief and well organized. The description of Raynaud's disease is excellent and the limitations in surgical treatment are given. The various operations for essential hypertension are discussed and realistic criteria on which patients should be selected for this operation are given. Other conditions discussed include hyperhidrosis, causalgia, and pain. The technique of sympathectomy is described and illustrated. The author's purpose in writing this book was to indicate that there is a rational basis for every sympathectomy and he has succeeded. This book should have its greatest use by those surgeons who are frequently asked to consider one of the operations on the various parts of the sympathetic nervous system for the myriads of conditions that are affected by the autonomic nervous system. Both the usefulness and the limitations are honestly stated.

Treatment of Lung Cavities and Endobronchial Tuberculosis, with Special Reference to Treatment in Malaya. By Beryl E. Barsby, M.D., M.R.C.P. Boards. $4.75. Pp. 147, with 46 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 & 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

This small volume records the experiences with pulmonary tuberculosis by physicians of excellent qualifications under primitive conditions in Malaya as it is today, a country of widespread disease. The experiences of the staff physicians at the General Hospital at Johore Bahru are recorded in detail. The authors elucidate a condition first described by Carswell in 1838 and about which Zurik noted "Even in 1954, the true involvement of the trachea and bronchi in pulmonary tuberculosis is far from clear, . . . its frequency is still greatly underestimated." Some physicians, although aware of the condition, are not fully conversant with the important part it plays in the treatment of the patient. Even if surgery is not contemplated, the author hopes that this work will clarify certain points and help other workers in the field to understand some of the problems which confront the physician. This study was confined to adults among a population suspicious of modern methods of treatment. Though the patients were later extremely cooperative, a full follow-up system was difficult to attain in a country where communications are poor by modern standards.

The chapters are comprehensive and deal with the social background of Malayans; hospitals, the people, epidemiology, and the problem of endobronchial tuberculosis; histology related to bronchoscopic appearances; incidence of disease; symptoms and signs; pathogenesis; radiologic observations; physiological relationship of bronchial tuberculosis and cavities; effects of drugs; healing and treatment; management of cavities; surgical aspects; management of pyopneumothorax; anesthesia for bronchoscopy; and physiotherapy. This book deserves reading by virtue of its fine observations on endobronchial tuberculosis, its clear description of an area rampant with tuberculosis, and its good quality throughout.

Safe Handling of Radioisotopes. Safety series no. 1. [Also published in French, Russian and Spanish.] Paper. $1; 6 shillings; 350 French francs. Pp. 99. International Atomic Energy Agency, Kärtner Ring, Vienna I, Austria, 1958.

This booklet offers detailed and specific instructions for the handling of both sealed and unsealed sources of ionizing radiation. The importance of organizing, planning, monitoring, and record-keeping is stressed in the introduction. Valuable technical hints are given as to shielding, design of work places, protective clothing, ventilation, storage, transportation, and waste disposal. Two special sections deal with accidents and decontamination. Appendix I gives the accepted figures for permissible doses of radiation with definitions of the terms and units essential in applying the data. Appendix II gives maximum permissible levels for surface contamination of equipment, work places, clothing, and skin. The book dispenses with illustrations, but readers will appreciate the succinctness of the text.

Pathology. By Peter A. Herbut, M.D., Professor of Pathology, Jefferson Medical College and Director of Clinical Laboratories, Jefferson Medical College Hospital, Philadelphia. Second edition. Cloth. $18.50. Pp. 1516, with 1506 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1959.

This edition has been increased by 288 pages and 213 photographs. The portions on the general pathological processes have been revised with greater emphasis on mechanisms and pathological aspects. A section on the systemic pathology of the organ or system discussed has been added at the beginning of each chapter. Wherever possible the subject material has a brief summary of the normal physiology; a discussion of specific and less specific deviations from the normal; a correlation, when possible, of morphology and physiology; and a discussion of tests by which altered physiological function can be discerned. The large content of text material is presented in 40 chapters, 7 of them devoted to general pathology as follows: orientation, the autopsy, congenital anomalies, degeneration, *inflammations*, physical disturbances, and tumors. The chapters on systemic pathology deal with the heart; vessels; upper respiratory system; larynx; lower respiratory system; thyroid; parathyroids; upper digestive system; esophagus; stomach; small intestine; appendix; colon; liver and biliary system; pancreas; peritoneum; reticuloendothelial system; blood; spleen; lymph nodes; thymus; adrenals; lower urinary system; breast; bones; joints; fascias, tendons, and bursas; skeletal muscle; skin; and central nervous system. Each chapter has detailed instructions or descriptions pertinent to the topic. The book is well written in a clear direct style; the illustrations are well chosen and of good quality. Suitable bibliographies are given at the close of each chapter. The book is recommended to students in medical schools, residents in specialized training in pathology, and others.

The Treatment of Diabetes Mellitus. By Elliott P. Joslin, A.M., M.D., Sc.D., Physician, New England Deaconess Hospital, Boston, Howard F. Root, M.D., H.H.D., Medical Director, Joslin Clinic, Priscilla White, M.D., Sc.D., Physician, New England Deaconess Hospital, and Alexander Marble, A.M., M.D., Physician, New England Deaconess Hospital. With cooperation of Dr. Robert F. Bradley and others, and associates in Joslin Clinic and Baker Clinical Research Laboratory, New England Deaconess Hospital. Tenth edition. Cloth. $16.50. Pp. 798, with illustrations. Lea & Febiger, 600 Washington Sq., Philadelphia 6, 1959.

Joslin's book continues to be the vade mecum of the physician interested in diabetes. Strictly speaking, it is less Joslin's book than it used to be, for in addition to the co-authors of the earlier editions there now appear a number of new collaborators. Several chapters, however, were written by the senior author alone. They bear his unmistakable imprint and remind one that he has his hand firmly on the helm. This very useful book represents an accumulated experience with more than 50,000 diabetic patients; an experience extending back into the last century, yet it is fully up to date in its inclusion of the latest developments. Among the new contributions are those on physiology by Renold, and on acidosis by Nichols and Root, which are outstanding. The oral methods of treatment are discussed competently and conservatively by Marble and Krall. The degenerative complications receive much attention, since cardiovascular-renal disease has increased steadily, and now accounts for 77.7% of all deaths of diabetic patients. Ditzel, a co-author of the chapter on ocular disease, has studied the small vessel pattern of the bulbar conjunctiva of living subjects with the aid of the stereoscopic dissecting microscope. He describes abnormal patterns in children who have incipient diabetes long before retinopathy is discernible and in 35 to 43% of children of diabetic mothers, as well as in both younger and older patients, with well-established diabetes.

The Joslin group has yielded no ground in its contention that good control of glycosuria tends to prevent vascular disease, while poor control favors it. In support of this contention, they cite their "Victory medal" patients, now numbering 88, who have had well-controlled diabetes for 25 years or more and show no such complications. They refer also to impressive studies reported previously, in which most long-term patients under good control were found to have little or no retinopathy or nephropathy, while most of the poorly controlled patients had severe lesions. Here, however, as in the original reports, the authors regrettably take no cognizance of the sizable minority which, in each group, constitutes an important exception to the rule and in whom factors other than control must be involved. If it is true that dietary fat plays some role in the genesis of atherosclerosis, it would seem to have special pertinence for the diabetic, who has a tendency toward hyperlipemia, anyway, and whose fat intake traditionally has been high because the carbohydrate intake has been low. Such considerations lead the authors to recommend that calories from fat be kept at less than 40% of total calories and that polyunsaturated fats replace animal fats to as great an extent as is feasible. More drastic modifications of diet are not advised.

The book has very few faults. There is some duplication of material in chapters written by different authors, but this is hardly objectionable. The maximum activity of protamine zinc insulin is given as occurring at 8 to 12 hours in one place (page 285) and 12 to 24 hours in another (page 664), the latter being more in accord with general experience. An undue amount of space is given to trauma. The chapter on pregnancy, in which the case for the use of female sex hormones is presented in somewhat new form but with undiminished enthusiasm, is rather dogmatic in some places and occasionally clarity and readability seem to have been sacrificed for brevity.

A Practice of Thoracic Surgery. By A. L. d'Abreu, O.B.E., Ch.M., F.R.C.S. [Second edition.] Cloth. $19. Pp. 619, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-42 Maddox St., London, W. 1, England, 1958.

The beauty of science is that it is rarely static and never complete. The fault inherent in all textbooks is that they present the subject as it was a year or more before the date of publication. This does not mean that textbooks are not necessary. For the student and for the busy practitioner they provide a compact body of knowledge which, if the particular science is not progressing too rapidly, will give them a basic understanding of the subject and serve as a basis for their reading in the current literature. The ideal textbook avoids this fault and fulfills its purpose by presenting each subject historically, showing how and why it has evolved, and by so doing emphasizing the fact that it *is* still evolving; its great virtue lies in its complete bibliography and in the skill with which a body of literature has been digested and condensed. This type of textbook is a labor in objective scholarship. There is another type of medical textbook, of which the work under discussion is an excellent example, which is also valuable; it presents the current practice and opinion of a single person or of persons connected with a clinic. If these persons are abreast of the times and have the wide experience afforded by years of practice, the textbook should be good. It should be valuable to the student and also of great interest and value to those practicing the specialty of thoracic surgery.

In the introduction to this book, the author states frankly that it is "a" practice of thoracic surgery and not "the" practice. Because he is familiar with what has been done and said in this field and because he has had a wide experience in it, the book presents a good picture of the subject as it is practiced throughout the world. No thoracic surgeon will find much to disagree with or criticize. Everyone, however, is bound to discover some points which, in his opinion, are minor sins of omission and commission. Too little space has been devoted to crushing injuries of the chest. No mention is made of soft tissue traction or the use of the mechanical respirator. In discussing thoracoplasty for pulmonary tuberculosis, the author fails to mention subscapular extraperiosteal paraffin plombage and he is perhaps too ready to classify artificial pneumothorax as a permanently obsolete procedure. These are minor criticisms. This major contribution is excellently written and the illustrations are good and adequate. It is probably the best textbook on the subject of thoracic surgery available today.

Pharmakologie als theoretische Grundlage einer rationellen Pharmakotherapie. Von Knud O. Møller, Professor der Pharmakologie an der Universität Kopenhagen. [Third German edition translated and edited from fifth Danish edition by O. Walker.] Cloth. 65 Swiss francs; $16.25. Pp. 902, with 50 illustrations. Benno Schwabe & Co., Basel 10, Switzerland; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1958.

This is the third German edition, prepared from the fifth Danish edition, of a magnificent textbook of pharmacology. The preface lists the many sections that have been added since the second German edition. The list, too long to reproduce here, includes insect repellents, detergents, emulsifiers and macrogoles (polyethylene glycols of various molecular weights), antimorphines, new urea derivatives, carbonic anhydrase inhibitors, new antidiabetic drugs, ion exchangers, phenindione and other new anticoagulants, and tetracemin and other new chelating agents. Many other sections have been drastically revised. There is an up-to-date bibliography and a good index. In spite of the large size of the work and the rapid rate of change in its subject matter, the facts have been well assimilated and are clearly presented. The simple directness of the German does credit to the translator and will be appreciated by American readers. The book merits the attention of pharmacologists everywhere.

Tuberculosis and Other Communicable Diseases. [Edited] by J. Arthur Myers, M.D., Professor of Internal Medicine and Public Health, Medical, Public Health and Graduate Schools, University of Minnesota, Minneapolis. With introduction by Irvine McQuarrie, A.B., Ph.D., M.D. Cloth. $14.50. Pp. 499, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

When the countless advances by medical science during recent decades are appraised in the light of their total impact on human welfare, the most impressive and significant will be concerned with the field of infectious diseases. Many of these achievements are reviewed in this volume in contributions by leaders in their special subjects. The editor is a well-known specialist in public health and preventive medicine whose studies in tuberculosis are outstanding. The present volume fulfills the desire to center attention on the communicable nature of tuberculosis and comparable infectious diseases. This and the concept of early recognition and prompt isolation in prevention of such diseases should make the volume useful to the medical student and practitioner, as well as a textbook in nursing and public health courses. Much preventive work remains to be done even though diagnostic, therapeutic, prophylactic, and epidemiologic measures are well established. None of these diseases has been eradicated and many remain constant threats to every community. Myers cites a smallpox epidemic with 300 deaths, due to lack of information, economic situations, and cultists who opposed preventive measures. If the information presented in this book is adequately disseminated and used, people may live longer, more happily, and more efficiently than preceding generations. The chapters cover tuberculosis, systemic mycoses, acute respiratory diseases, viral diseases, brucellosis, common cold, poliomyelitis, rheumatic fever, meningitis, impetigo, gonorrhea and syphilis, and others. The volume should be in demand among medical students, general practitioners, nurses, public health workers, and all concerned with communicable diseases. It is presented in simple and plain language.

QUESTIONS AND ANSWERS

LIGHTERS AS LUNG CANCER FACTOR

To the Editor:—*Has the possible role of the cigarette lighter as a cause of lung cancer been considered? The lighter may be suspected in view of the facts that cigarettes appear to be blamed more than pipes or cigars and that fumes from the lighter and its fuels might not be trapped in a cigarette. Cigar and pipe smokers may use mechanical lighters too, but not as often. One pack of cigarettes a day would mean 20 lights. Could such fumes cause lung cancer?*

N. F. Slomer, M.D., Cincinnati.

Answer.—It is reasonable to assume that fumes of a cigarette lighter may be a factor in the etiology of lung cancer in a way similar to that of atmospheric deposit and smoke. However, other factors are apparently more significant. For example, in England, where the death rate from lung cancer is higher than in any other country, the cigarette lighter is probably not nearly as widely used for economic reasons as in the United States. In an excellent study of the relationship of cancer to atmospheric deposit and smoke (*Brit. M. J.* 1:74, 1959), Stocks points out that, although there is a much higher incidence of lung cancer and bronchitis in urban as compared to rural areas in England, there was no urban excess for heavy cigarette smokers. According to Doll (*Brit. M. J.* 1:322, 1959), there is a distinct relationship in 16 countries between the reported cigarette consumption in 1930 and lung cancer death rates in 1952 to 1954. A striking exception is the United States, which had a relatively high cigarette consumption but a relatively low incidence of cancer of the lung, in spite of the popularity of the cigarette lighter in this country. A possibly significant additional factor is that the average pipe or cigar smoker is much less likely to inhale the smoke.

POISONOUS MUSHROOMS

To the Editor:—*Is it true that the poisonous mushroom, Amanita phalloides, is not found in North America?*

A. L. Springer, M.D., Philadelphia.

Answer.—Amanita phalloides has been reported growing in most sections of the United States but is most commonly found in the northeastern part of the country. Many cases of poisoning from this species have been reported in the United States, but, because of problems of identification, some poisonings attributed to this species may have been caused by other species of Amanita (Amanita verna or Amanita brunnescens) which contain the same toxin and produce symptoms similar to those of poisoning by Amanita phalloides.

DIABETES SURVEY IN SCHOOL

To the Editor:—*At a recent medical staff meeting, it was decided to secure information on detecting diabetes in school children. Please give advice as to the value of such a program by urine test.*

G. H. Spurbeck, M.D., Bemidji, Minn.

Answer.—The incidence of juvenile diabetes is low—1 per 2,500 children under the age of 15 years. The most profitable case finding will be among relatives of diabetics. The best procedure to follow would be postprandial urine tests, then, if positive, postprandial determination of blood sugar level, and, finally, a glucose tolerance test. Early cases have been diagnosed in school surveys, and it is advantageous to recognize these persons in the preclinical period. Glycosuria not due to diabetes is extremely common in children and many tests may be performed which would be insignificant, but a single case diagnosed early is worth the effort.

LEPTOTHRIX AND STREPTOTHRIX CULTURE

To the Editor:—*A boy has leptotrichosis of the conjunctiva (Parinaud's conjunctivitis) believed to be due to a Leptothrix. The pathologist has been unable to culture it. A consultant has stated that there is a special technique for cultures and smears to demonstrate the organism, but he is not familiar with it. Another patient has a corneal ulcer believed to be due to a fungus, and, again, the organism has not been demonstrable but it is thought to be a Streptothrix. Please give instructions on how to demonstrate these organisms by smear, biopsy, or culture. What is the treatment, if any, and how effective is it?*

C. T. McCoy, M.D., Hutchinson, Kan.

Answer.—Streptothrix and Leptothrix organisms are best isolated from the eye by the removal of concretions in the lacrimal sac or canaliculae. Corneal lesions should be scraped. The Streptothrix is anaerobic and may be grown on peptone glyc-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

erine agar (Breed and others, Bergey's Manual of Determinative Bacteriology, ed. 7, Baltimore, Williams & Wilkins Company, 1957). If biopsy is possible, the lesion will consist of loose granulation tissue composed of epithelioid, lymphoid, and polymorphonuclear cells with many giant cells, among which are scattered necrotic areas containing the organisms. Streptothrix is a filamentous fungus with branching ends as distinguished from the Leptothrix, which is unbranched. Streptothrix is also gram-positive and turns blue in the presence of Gram's stain. The organism responds somewhat to sulfonamides, penicillin, thymol in a 1:1,000 solution given locally, and iodides given locally and by mouth. Leptothrix is rather difficult to isolate. Culture may be accomplished on dextrose-serum-agar with rigid attention to the partial oxygen tensions (Verhoeff and King, *Arch. Ophth.* 9:701, 1933). Treatment is the same as for Streptothrix.

FOOD ADDITIVE

To the Editor:—*Dream Whip, a General Foods product, contains "propylene glycol monostearate." Are there any toxic effects from this chemical when added to food?*

Solomon Goodman, M.D., Brooklyn, N. Y.

Answer.—This consultant is unaware of any toxic effects to be expected from the ingestion of this product. Use of propylene glycol monostearate is permitted by the Federal Food and Drug Administration. Records do not indicate it may be harmful. Detailed information regarding it can be obtained from the Food Protection Committee, Food and Nutrition Board, National Research Council, 2101 Constitution Ave., Washington 25, D. C.

ERGOTISM WITH MIGRAINE

To the Editor:—*A patient who received ergotamine tartrate injections and ergotamine-caffeine suppositories for migraine headaches that occur every other day developed circulatory symptoms of ergotism in one leg. Is there any other appropriate treatment? Is there some way of combating the ergotism? The patient is also receiving psychoanalytic treatment.*

Ralph M. Crowley, M.D., New York.

Answer.—Ergot and its alkaloids are the sovereign treatment of actual migraine attacks. However, caution should be exercised in the use of ergotamine in any form. A patient who has migraine attacks every other day and receives the treatment described probably will develop symptoms of ergotism sooner or later. Long-term administration of the drug may often produce central symptoms, with headaches and giddiness, in addition to peripheral symptoms of ergotism. Instead of the ergotamine, dihydroergotamine could be tried with this patient. It is less toxic but somewhat less effective in combating the actual migraine attack. Therefore, its dose should be about twice that of the ergotamine. If the patient has already developed symptoms of ergotism, ergot and its alkaloids are definitely contraindicated and their administration should be stopped. If the symptoms of ergotism do not disappear after this, vasodilators, such as choline esters, nitrites, papaverin, and cyclandelate, in 100-to-200-mg. doses, should be tried to correct the peripheral effects. Large doses (100-500 mg.) of nicotinic acid, which is a potent peripheral vasodilator, should be useful. Instead of the ergotamines, 30-to-60-minute inhalations of 100% oxygen, which the patient could administer to herself while in bed, should be tried. Some of the newer analgesics, such as dextro propoxyphene hydrochloride, in a dosage of 65 mg. four times daily, may be useful in combating the pain connected with the migraine attacks. Because the patient suffers from migraine attacks every other day, reexamination and reevaluation of the migraine should be attempted. The migraine attacks themselves might be psychogenic due to frustration or might be a symptom of allergy. If they are due to allergy, proper desensitization should be tried. If the attacks are purely psychogenic, the psychoanalytical procedure itself may aggravate the condition. If this should prove to be the case, then use of the abreactive technique with sodium amytal or ether should be tried. If the patient reacts to the abreactive technique with a benign catharsis, the psychoanalytic procedure may be resumed later if desired.

GASTROINTESTINAL CHANGES IN MALNUTRITION

To the Editor:—*What x-ray characteristics are found in the gastrointestinal tract in patients with malnutrition, avitaminosis, and starvation?*

N. B. Jaffe, M.D., Bridgeport, Conn.

Answer.—The question refers to conditions now generally grouped together as the "malabsorption syndrome" (Combined Staff Clinic, *Am. J. Med.* 15:790, 1953). These conditions in some patients produce, or at least are associated with, a disorder of motor function in the small intestine manifested by hypotonicity and slow transit time. If a barium-water suspension is used, flocculation or "clumping" of the barium may occur. If nonflocculating barium preparations are used, the caliber of the lumen may be wider and progress of the opaque material may be slower than average but normal limits are difficult to define. Emptying of the stomach may be slow because of inadequate peristalsis. Evidence has been produced that these disorders of motor function are based on inadequate production of acetylcholine in the tunica muscularis. In advanced cases, both the mucosa and the muscle coat may be found atrophic at autopsy. In uncommon instances, the mucosal folds of the jejunum (valvulae conniventes), as shown on barium examination, may be reduced in number or in height or may be obliterated, leaving the inner surface of the intestine smooth. With proper treatment these motor disorders disappear, but they are irreversible in some advanced cases.

Disturbances in motor function of the intestine, similar to those found with milder nutritional disorders, have been seen in patients who are emotionally disturbed. In advanced nutritional disorders, gas distention of the intestine may simulate ileus. This has been described in sprue. It occurs in southern India among poor persons whose diet consists largely of a preparation of millet, and it may be fatal if dietary treatment is delayed. In the United States, cases of gas distention have been reported in which ileus was simulated and in which the disorder responded to vitamin treatment (Leithauser, *Surg. Gynec. & Obst.* 86:543, 1948). Vitamin insufficiency may play a part in some cases of postoperative distention and paralytic ileus (Frazer and others, *J. A. M. A.* 169:1047-1051 [March 7] 1959). Hypoproteinemia and hypokalemia may cause gas distention which is promptly relieved when blood protein and potassium levels are restored to normal.

Variability of the effects on the intestine seems to depend in part on the severity and duration of the nutritional disorder and on the kind and amount of dietary treatment in the past. However, at present some of the vagaries in the manifestations of nutritional disorders in different persons cannot be explained. Starvation presumably refers to acute deprivation of food. No x-ray studies of such persons have been reported.

FAT AND LEAN FISH

To the Editor:—*Please give a list of fat and a list of lean fish.*

E. M. Meek, M.D., Greenwood, Miss.

Answer.—Fat content of fish may vary from less than 1% to more than 12%. The amount of fat in all fish varies somewhat with the season of the year, with the time of spawning, and with changes in feeding conditions. The table, from the book "Nutrition in Health and Disease," by Cooper and others (Philadelphia, J. B. Lippincott Company, 1953), lists the two categories.

Fat Content of Fish, Percentage

Fish Low in Fat		Fish High in Fat	
Bass	2	Bonito	7
Cod	Trace	Herring	13
Flounder	1	Mackerel	12
Haddock	Trace	Salmon, Pacific	17
Pike	1	Shad	10
Trout, brook	2	Whitefish	7

BIFOCALS IN CHILDREN

To the Editor:—*Bifocal lenses are being prescribed for teen-agers and younger children. What are the reasons for prescribing bifocal lenses other than loss of accommodation?*

H. B. Jenkins, M.D., Chandler, Okla.

Answer.—Bifocal lenses are useful in management of the following ocular problems in children: 1. Paralysis of accommodation. This may occur after diphtheria and measles with encephalitis or in children with brain damage. 2. Motor imbalance. The child with an esotropia which is greater at a distant focus than at near focus might be greatly helped by bifocals. Accommodative spasm resulting in an intermittent esotropia will also be helped. 3. Subnormal vision. The child with subnormal vision may use bifocal lenses to provide magnification for near vision. Bifocal lenses in children play an important part in the management of ophthalmological problems. Their acceptance by parents, teachers, and other children should be encouraged by all physicians.

SEA WATER BY RECTUM

To the Editor:—*Is it theoretically possible to maintain the water requirements of the body by instilling ocean water into the rectum? Are there any records of this having been done in an emergency, such as shipwreck, with absence of potable water, in the otherwise healthy adult?*

M.D., Georgia.

Answer.—The question is aptly answered by Critchley in his book entitled "Shipwreck Survivors" (London, J. & A. Churchill, Ltd., 1943, p. 96): "From time to time the suggestion is made that thirst might be relieved and dehydration prevented by the instillation of salt-water into the rectum. A short note in the medical press during the last war suggested that a Higginson's syringe should be part of a lifeboat's equipment. On theoretical grounds, such a practice would appear to be very undesirable, with great risk of producing purgation and increased dehydration. Allison and Critchley instilled sea water per rectum on six occasions in two cases of diabetes insipidus. Thirst was not relieved and in one subject considerable discomfort was produced. Recently Foy, Altmann and Kondi carried out similar experiments on healthy volunteers who were taking no water by mouth; they found that although sea water is absorbed from the rectum, it does not relieve the objective signs of dehydration and haemo-concentration. They found that the subjects who had sea-water enemas lost more weight than those who were simply starved of water. The chlorides, too, rose higher and they thought there was a risk of harm in bringing about still higher grades of tissue dehydration."

SUBCUTANEOUS ADMINISTRATION OF DEXTROSE SOLUTION

To the Editor:—*Is the subcutaneous administration of hypertonic (10%) dextrose solution justified and, if not, why not? Dextrose in distilled water or isotonic sodium chloride solution has been given subcutaneously with hyaluronidase as a diffusing agent when venoclysis was difficult or impossible, and no local or systemic ill effects have been observed.*

L. A. O'Donnell, M.D., Wichita, Kan.

Answer.—There is little to indicate that the subcutaneous administration of hypertonic (10%) dextrose in isotonic sodium chloride solution would do any harm. However, whether it is as easily absorbed as a 5% solution, which is isotonic, is debatable. The subcutaneous injection of hypertonic solutions of dextrose involves its absorption, balance of water, inorganic constituents of the body fluids, and the state of nutrition. There are situations in which a 10% solution of dextrose seems to be optimal, but, under usual considerations, use of a 5% solution would be preferred.

CORNSTARCH INHALATION

To the Editor:—*A man, aged 32, works in a printing shop where cornstarch powder is blown onto each freshly printed sheet. Because of severe cough, twice in the past year he has had bronchoscopic study which has revealed thick mucus in the lower bronchi. Microscopic examination of the washings shows no eosinophils, cells, or pathogenic organisms. All other laboratory reports are normal. Bronchograms are normal. Is the cornstarch responsible for the cough?*

G. H. Nadeau, M.D., Riegelsville, Pa.

Answer.—It is doubtful that the cornstarch powder is responsible for the condition described. Cornstarch powder is a bland material and is not in itself irritating. The quantity involved is not enough to cause any chronic irritation or be likely on inhalation to reach deeper pulmonary surfaces. The possibility might well be investigated that some other substance capable of producing an allergic reaction and subsequent severe cough is a factor in this case.

DIVERTICULOSIS

To the Editor:—*Please give information, particularly experimental data, as to the pathogenesis of diverticulosis of the gastrointestinal tract.*

Alan A. Kane, M.D., Brooklyn, N. Y.

Answer.—A discussion of the pathogenesis of diverticulosis of the gastrointestinal tract is beyond the necessary space limitations of this department. Most of the data available is derived from anatomic observations only; this consultant is familiar with no experimental work on the subject. The inquirer is referred to the article by Welch (*DM*, June, 1958), which gives a complete discussion of the subject.

WITHDRAWAL OF ADRENAL STEROIDS

To the Editor:—*About one year ago, a 38-year-old woman with scleroderma was given three tapered courses of prednisone therapy lasting four to six weeks with rest periods between. The total duration of treatment was six months, and the total prednisone dosage administered was about 400 tablets of 5 mg. each. Potassium chloride and meprobamate were given in conjunction with the prednisone. The only side-effects encountered during the treatment consisted of slight moon face, hirsutism, spindle legs, potbelly, scant menses, palpitation, and emotional lability. After prednisone therapy was withdrawn completely, the following symptoms persisted: restlessness, emotional lability, memory deficit, anorexia, asthenia, fatigue, and palpitation; stress symptoms, with the slightest exertion followed by palpitation, dyspnea, and perspiration alleviated only by rest (the patient feels best in the morning but is completely exhausted after being up and about for two hours, and she has to rest in bed three times during the day); and pseudorheumatism with tenderness of muscles and bones (sternum, heels, and skin over most bony prominences) improved by rest and aggravated by activity.*

It is now six months since steroid therapy was stopped. The original moon face, hirsutism, and thinning of leg muscles are now absent. Menses alternate between scant and heavy and are regular. The patient has taken meprobamate alone for the past six months and requires 800 mg. four times daily to control the emotional lability, palpitation, and tenderness of muscles and bony surfaces. Her appetite is good, and improvement has been gradual but slow. She is still totally incapacitated as far as productive employment is concerned and is confined to her home. Consultants in internal medicine advise no specific treatment and have indicated that, usually, in six months spontaneous return of adenopituitary function occurs. The six months have passed. How much longer are the present symptoms likely to continue to an incapacitating degree? Is any specific corrective or substitution treatment indicated?

M.D., California.

Answer.—One wonders if the symptoms which persist six months after termination of steroid therapy are actually related to depression of pituitary and adrenal function. This seems unlikely, in view of the fact that there is usually good recovery of this function after six months or less, particularly if the therapy with steroid hormones was intermittent, as in this case. Furthermore, relief of some of the symptoms with meprobamate suggests that emotional factors may be playing an important role. An evaluation of adrenocortical function could be made by means of estimations of the urinary 17-ketosteroid and corticosteroid and the plasma corticosteroid levels, if facilities for the latter determination are available. It should be remembered that not much significance should be attached to a low excretion of 17-ketosteroids in a chronically ill patient. In any event, no specific treatment from the standpoint of the pituitary or adrenals seems indicated. Further treatment with steroids is probably not desirable, as this would only prolong suppression of adrenocortical function if this were currently a problem. Likewise, adrenal stimulation with ACTH has little value in this sort of situation. As a general rule, only the passage of time will permit recovery of normal pituitary and adrenal function after prolonged suppression by steroids, and replacement therapy is usually not indicated except in stressful situations, such as surgical operation, trauma, or febrile illness.

OILY SKIN

To THE EDITOR:—*Is there a direct relationship between the lipid and the cholesterol content of the blood and the oiliness noted on the skin? Is oily skin inherited?*

M.D., Tennessee.

ANSWER.—There is no evidence of any direct relationship between lipid and/or cholesterol contents of the blood and oiliness of the skin. Excessive oiliness of the skin, such as observed in seborrhea oleosa, apparently has an intrinsic, largely endocrine and familial basis.

TREATMENT OF FLAT FOOT

To THE EDITOR:—*Please give information on methods of treatment for flat foot. What kind of arches and shoes should be prescribed? Please suggest some references.*

Donald R. Gibbs, M.D., Cortland, N. Y.

ANSWER.—The problem of flat foot is not simple. The causes are manifold and may be congenital or acquired. It may occur after infection, injury, or paralysis. The most common form is the so-called static flat foot. This is the result of foot strain. The foot is decompensated. This means the work demanded of the foot is greater than the strength of the foot. Thus, lack of exercise, such as normal walking, can be a causative factor. At the same time, prolonged standing can be a factor. Ill-fitting shoes that interfere with normal functions are an important factor. There are many other factors, all of which would have to be taken into consideration in the treatment.

Flat foot is the result of alterations in the relationship of the bones to each other. The heel goes into valgus and the mid-position of the foot is pronated, thus lowering the longitudinal arch. Correction requires elimination of the causative factors. It is necessary to bring the heel into varus and correct pronation of the foot, thus restoring its normal position. With the foot in proper position, normal function must then be reestablished. A technique for doing this is described in "Diseases of the Foot," by Hauser (Philadelphia, W. B. Saunders Company, 1950). Another method is described in "Functional Disorders of the Foot: Diagnosis and Treatment," by Dickson and Dively (ed. 3, Philadelphia, J. B. Lippincott Company, 1953).

ROENTGEN EPILATION

To THE EDITOR:—*Is roentgen epilation of the scalp justified in patients with ringworm which fails to respond to any other form of therapy? Have there been any long-term comprehensive follow-up studies in such cases?*

John B. Light, M.D., Lebanon, Pa.

ANSWER.—The usual epilating dose of x-ray does no known damage to the growing hair follicles. Provided the scalp is subjected to no more than the minimal effective threshold dose, there should be no undue concern about permanent latent epilation, blanching of the hair, or other damage. This consultant knows of no follow-up studies on effects of radiation to the scalp. If the dose is kept within proper limits, there should be no latent effects.

YOGHURT

To THE EDITOR:—*What bacteria are found in yoghurt? Is anything known about the bacteriology of a culture of yoghurt that supposedly came from a Canadian monastery which is reported to be the source used by most American dairies?*

M.D., Oregon.

ANSWER.—The characteristic organism of yoghurt is Lactobacillus bulgaricus, although others may be present. Variations in flavor of yoghurts from different sources are due in part to the presence of different micro-organisms. L. bulgaricus was isolated by Grigoroff in 1905 from Bulgarian fermented milk. Metchnikoff suggested that this organism would be a valuable addition to the intestinal flora, but, according to Jordan and Burrows (Textbook of Bacteriology, ed. 14, Philadelphia, W. B. Saunders Company, 1945, p. 484), it does not become implanted in the intestine. This consultant has no information concerning the yoghurt supposed to have come from a Canadian monastery. The nutritive value of yoghurt is almost the same as that of the milk from which it is made. No unique nutritional or therapeutic properties are known that can be attributed to it.

WASHINGTON NEWS

Forand Bill Status . .
Senate Urged to Help Nursing Homes . .
International Medical Research . .
Government Employees' Health Insurance . .
Further Hearings on Problems of Aged . .

FORAND BILL PROSPECTS

The controversial Forand bill to add health care for the elderly to the Social Security system may not be acted on by Congress this year. After the House Ways and Means Committee ended five days of hearings on the measure in July, supporters of the bill said they did not expect action until next year. Sponsor of the legislation, Rep. Aime Forand (D., R. I.), said, "in view of the heavy agenda of the committee, I don't think we will be able to get this legislation to the floor before adjournment this session."

The administration, the American Medical Association, and numerous other organizations have urged the lawmakers to reject the bill on the grounds that the problem is being solved on the local level, that the bill would lead eventually to complete federal control of medicine in this country, and that it would cancel the progress made so far through private, voluntary means.

Representative Forand said after the sessions that he realized the hearings on the subject were not conclusive and that he was open to any alternative proposal that would work. He suggested that the subject of health care for the elderly be reviewed thoroughly, perhaps by a special subcommittee that would hear from all interested groups.

One of the final witnesses was Dr. R. B. Robins, a member of the Board of Trustees of the American Medical Association. He testified on behalf of the American Academy of General Practice. He declared that the Forand measure is compulsory national health insurance on a limited scale. If it became law, he testified, compulsory national health insurance for everyone could soon result.

Dr. Robins described the quality of medical care he found in England on a recent trip. He said that in his opinion the quality has obviously deteriorated, with long queues of patients waiting for hours to see physicians. Medicine in England, he said, is practiced on an assembly-line basis and is a cold, impersonal process. Physicians there are dissatisfied and are leaving the country, said Dr. Robins.

Another witness, E. J. Faulkner, testifying on behalf of the Health Insurance Association of America, said that addition of health care benefits to federal old age and survivors disability insurance benefits "would retard the rapid progress of voluntary health insurance and impose an increasingly heavy tax burden on workers and employers."

The cost of the program, he said, would be enormous—ranging from 2 billion dollars for the first year to 7 billion dollars by 1980. Eventually old-age tax deductions would amount to between 10 and 15% of payrolls, Faulkner testified.

Dr. F. J. L. Blasingame, executive vice-president of the A. M. A., said after the hearings that "the medical profession welcomed the opportunity to demonstrate to Congress that, although things are not perfect, much progress has been made in meeting the health care needs of the aged without intervention by the federal government.

"It was shown that it would be most unfortunate for the federal government to move in for political reasons and attempt in a compulsory fashion to solve by legislation problems which are being thoughtfully considered at the state and local levels by the medical profession and other dedicated members of the health team.

"Spokesmen for state medical societies, in testimony and statements for the record, reported encouraging progress. It added up to a creditable record.

"If government intervention, along the lines of the Forand bill, should occur, it would result, unfortunately, in the end of many of these voluntary programs."

A. M. A. URGES NURSING-HOME PROGRAM

The American Medical Association asked Congress to approve an insured loan program for proprietary nursing homes as part of any over-all housing measure before the lawmakers.

In a letter to a Senate banking subcommittee, which is starting a new round of sessions on housing legislation, Dr. F. J. L. Blasingame, A. M. A. executive Vice-president, said the A. M. A. actively supported the nursing-home provision [illegible] atch-all housing bill vetoed by [illegible] earlier this year.

"We believe there is a critical need for new and improved facilities tailored to the specific health requirements of older citizens," said Dr. Blasingame in a letter to subcommittee chairman John Sparkman (D., Ala.). The American Nursing Home Association and other organizations, he said, "have accumulated evidence over recent years showing that they cannot provide service of the desired quality or quantity, because they are unable to obtain the credit they need on reasonable terms to permit them to increase the number and size of adequate nursing-home facilities."

The provision would authorize guarantees by the Federal Housing Administration of loans for construction or improvement of proprietary nursing homes. Dr. Blasingame declared that there is an immediate need for such guarantees for proprietary homes, "since according to the latest statistics over 70% of nursing-home patients are cared for in such facilities."

The A. M. A. official also proposed eliminating a requirement in the previous housing bill that state Hill-Burton authorities decide whether there is a need for the guarantees. The program should be administered by the FHA, and it should be sufficient that the homes meet standards established by the state, he said.

INTERNATIONAL HEALTH MEASURE BACKED

A House commerce subcommittee launched hearings on the Senate-passed bill establishing a 50-million-dollar international medical research program. Witnesses at the first round of hearings urged congressional approval of the measure, not only to spur medical knowledge but to improve international relations.

The administration's views were scheduled to be presented at a second series of hearings starting early in August. Arthur S. Flemming, Secretary of Health, Education, and Welfare, has opposed some provisions of the measure, including the flat 50-million-dollar yearly authorization.

One of the first witnesses, Dr. Howard A. Rusk, executive vice-chairman of Committee on Health for Peace, told the subcommittee, headed by Rep. Kenneth Roberts (D., Ala.), that the first-year cost for the research program would probably be only 10 or 15 million dollars. He noted that the fiscal year has already started and there would not be time to get the program into full operation for the entire year, even of Congress clears the bill this session.

Also supporting the bill were Gen. Omar N. Bradley, chairman of the Committee on Health for Peace, and Major Gen. Melvin J. Maas, chairman of the President's Committee on Employment of the Physically Handicapped.

General Bradley said the legislation would make it possible for the United States to support and coordinate medical research in foreign countries which could result in "pay-off" answers to killing diseases like cancer and heart disease.

In a statement to the subcommittee the American Medical Association reiterated its support of the measure.

HEALTH INSURANCE FOR GOVERNMENT WORKERS

The Senate overwhelmingly approved, by a vote of 81 to 4, a program of voluntary health insurance for United States employees. The House Post Office and Civil Service Committee immediately slated hearings on the legislation.

The twin actions enhanced prospects for passage of the measure this year. Despite administration opposition to some features of the Senate-passed bill, most Senate Republicans joined with the Democrats in voting for it.

The American Medical Association renewed its support of the principle of the legislation in a statement submitted to the House committee headed by Rep. Tom Murray (D., Tenn.). Dr. F. J. L. Blasingame, A. M. A. executive Vice-president, said the organization continues to endorse legislation which would authorize the Civil Service Commission to make available on a voluntary contributory basis group hospital, surgical, medical, and other personal health benefits for civilian officers and employees in the federal service.

The measure before the committee, he said, meets most of the suggested standards for a health insurance program drawn up by the A. M. A. Council on Medical Service and the Council on Legislative Activities.

Dr. Blasingame proposed two amendments which "can be made rather easily within the framework of this legislation." One would provide coverage on a voluntary, contributory basis for government workers who have already retired, and the other would eliminate a requirement that there be "one government-wide service benefit plan." Dr. Blasingame said, "we feel that the phrase 'one government-wide,' while intended to eliminate the necessity of the Civil Service Commission's entering into contracts with individual service benefit plans, is unfortunate.

"We know of no nationwide service benefit program which could meet the requirement of providing service to all federal employees. In a number of states, the Blue Shield programs operate indemnity plans."

One of the chief administration objections to the bill is the cost to the government—an estimated 145 million dollars a year, compared with the 105-million-dollar ceiling the administration had proposed.

HEARINGS ON PROBLEMS OF AGED RESUME

Sen. Pat McNamara (D., Mich.) called federal officials and spokesmen for national organizations to a series of hearings before his special Senate labor subcommittee in July and August to describe their activities in the field of aging and present their views and recommendations on needed action.

"The subcommittee will be concerned with such matters as whether present activities and policies are adequate to meet the needs of the aging and aged and the kinds of additional legislative action required," he said.

"There is a wealth of information in the experience and study of many voluntary organizations in this field, and we mean to benefit from their advice and consultation," he declared.

Some of the "top priority" problems the subcommittee will consider, he said, will include housing needs of the elderly, job discrimination, medical care, conditions of nursing homes, measures to prevent physical and mental deterioration, adequate income, and "elements of insuring a productive, meaningful life for those who retire from regular employment."

"If we continue our present practice of relegating older persons to the sidelines," said Senator McNamara, "the financial burden for the country in the way of institutions for the aged will be too fantastic to conceive."

"The time has long passed," he said, "for the country to be able to ignore this great domestic challenge of the midcentury. In the decades to come we should never allow it to be said that Americans—young and old alike—were foolhardy enough to waste the productive contributions of an expanding population of men and women reaching the age of 70 and beyond."

Advertisement

Pro-Banthīne®...what it will do and what it will not do...in Peptic Ulcer

Much consideration has been devoted ecently to a reappraisal of the role of nticholinergic drugs in the management of peptic ulcer.

Such reappraisal has presented no difculties at Searle. At no time have we uggested that Pro-Banthīne should be ubstituted for antacids, rest, psychoherapy or even common sense in manging the patient with peptic ulcer.

Action of Pro-Banthīne:

The action of Pro-Banthīne (brand of propantheline bromide) is simple and its ffects, allowing for the variability of the human estate, are predictable. Pro-Banthīne competes with and, in competing, inhibits the action of acetylcholine. This competition is highly effective at parasympathetic effector sites and, except with high dosage, somewhat less so at the autonomic ganglia.

Since parasympathetic nerves are moor and secretory to the stomach and motor to the intestines, Pro-Banthīne reduces both motility and secretions in the stomach and motility in the intestines. These actions have often been demonstrated experimentally and clinically.

What It Does:

Relieves Pain—One of the natural consequences of the actions of Pro-Banthīne is to reduce or to eliminate pain in peptic ulcer. Whether the pain is attributable to acid, to excessive motility or, to steer a middle course, to spasm induced by acid, the pronounced inhibitory effect of Pro-Banthīne on both secretion and motility might be expected to suppress the characteristic distress of ulcer.

In point of fact, relief of pain is one of the most prominent effects of Pro-Banthīne in peptic ulcer. Phrases such as "unexcelled" and "almost invariably effective" dot the literature referring to it.

Reduces Acidity—Since reduction of acid and rest for the hypermotile stomach and duodenum are accepted means of supporting the regenerative processes of the gastroduodenal mucosa, the physiologic modifications induced by Pro-Banthīne should be expected to have therapeutic implications in the healing of ulcers also. They do. Not only does Pro-Banthīne reduce gastric acid and motility but, through these actions, it also potentiates and prolongs the neutralizing property of antacids.

Aids Healing—Schwartz, Lehman, Ostrove and Seibel prescribed 120 to 180 mg. of Pro-Banthīne daily for 129 ulcer patients and found definite evidence, both clinical and roentgenographic, of accelerated healing.

With high doses (270 to 330 mg. daily) Barowsky, Schwartz and Lister reduced the mean duration of treatment in twenty-five patients with refractory ulcers from 135 to 17 days.

Helps Prevent Recurrences—Much the same considerations argue for the value of Pro-Banthīne in holding the reactivation of healed ulcers in abeyance, but the difficulty of regulating the diet, medication and mode of living of ulcer patients over long periods of time makes assessment of the role of Pro-Banthīne in preventing recurrences difficult. Nevertheless, in a study of 250 patients with established patterns of recurrence Texter and associates found that patients maintained on methantheline, less potent analogue of Pro-Banthīne, had significantly fewer recurrences than a control series taking atropine.

Schwartz and his co-workers considered freedom from symptoms when recurrences would be expected, together with tolerance and relief of symptoms, as a standard in establishing successful treatment in 118 of 129 patients.

Provides Selective Action—In inhibiting the action of acetylcholine in the stomach and intestines Pro-Banthīne also, though to a lesser extent, influences other cholinergically activated organs. That this influence sometimes leads to such secondary effects as dryness of the mouth, blurring of vision and hesitancy of urination is well known and bears consideration. It is one of the distinct advantages of Pro-Banthīne that it acts more effectively on the gastrointestinal tract than elsewhere. Secondary effects usually disappear during the course of treatment and only rarely limit therapy.

Evidence of selective action has been recorded by several investigators, but the most interesting confirmation of this selectivity was reported by Barowsky, Schwartz and Lister. They prescribed 30 to 45 mg. of Pro-Banthīne every hour and a half, except for the hour before and the hour following meals, for their patients with refractory ulcers. They were surprised and gratified by how few anticipated side reactions materialized. No serious toxic effects or side reactions occurred. The incidence of good response on double or triple the usual doses rose from 31 to 88 per cent.

Lowers Incidence of Failures—Variable results might be anticipated in a disease in which the psychic component plays such a large part and, of course, response to treatment does vary in patients with peptic ulcer. Observations of Lichstein and associates show that the 11 per cent of their patients who failed to respond to Pro-Banthīne had deeply ingrained anxiety on a psychoneurotic basis.

Successful management of such patients may well depend more on the patient's intelligence, the modification of his social environment and the skill of his physician in psychotherapy than on any medication. However, the successful experience of Barowsky and his colleagues in using large, frequent doses of Pro-Banthīne in patients with refractory ulcers might be borne in mind before Pro-Banthīne is abandoned as ineffective. Also worthy of trial in these patients is Pro-Banthīne® with Dartal® (brand of propantheline bromide with thiopropazate dihydrochloride), which combines the outstanding anticholinergic action of Pro-Banthīne with the highly efficient tranquilizing action of Dartal.

What It Will Not Do:

There are aspects of the medical management of peptic ulcer in which Pro-Banthīne has no demonstrable benefit. There is no reliable evidence that Pro-Banthīne reduces the incidence of complications or the need for surgery.

It will not abolish the obligation of physicians to evaluate each patient individually and to modify therapeutic measures to each patient's requirements. Nor will it do away with the necessity for the patient to regulate his life to the demands of his disease. But the modifying action of Pro-Banthīne on the physiologic activity of the gastrointestinal tract and its beneficial effects on the course of peptic ulcer have been established by too many investigators to be seriously questioned. Wisely used in conjunction with other standard therapeutic measures, Pro-Banthīne can inhibit pain, hasten healing and space out the intervals of peptic ulcer recurrence and do so without serious discomfort to the patient.

G. D. Searle & Co., Chicago 80, Illinois.
Research in the Service of Medicine.

REFERENCES:

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 *North Dearborn St., Chicago 10, Executive Vice-President.*

1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

August

American Association of Electromyography and Electrodiagnosis, Mayo Clinic, Rochester, Minn., Aug. 29-30. Dr. Edward Lambert, Mayo Clinic, Rochester, Minn., Program Chairman.

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, *Shirley-Savoy Hotel, Denver,* Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, *Suite 2115, Prudential Plaza, Chicago 1,* Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, annual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 C dral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor St. Louis County, Mo., *Sept. 18-20.* Dr. W. Payton Kolb, Baptist cal *Arts Bldg., Little Rock, Ark., Secretary.*

Mississippi Valley Medical Society, Hotel Chase, St. Louis, Sept Oct. 1. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19 L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Exe Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surg Chicago, Sept. 13-17. For information write the Secretariat, 1516 Shore Dr., Chicago 10.

Ohio Society of Anesthesiologists, Dayton Biltmore Hotel, Dayton, 18-19. Dr. Nicholas G. DePiero, 9710 Garfield Blvd., Garfield 25, Ohio, Secretary.

Oregon State Medical Society, Medford Hotel, Medford, Sept. Mr. Roscoe K. Miller, *1115 S. W. Taylor St., Portland 5, Ore.,* Exe Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Chairman.

United States Section, International College of Surgeons, House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt *City, Sept. 16-18.* Mr. Harold Bowman, *42 S. 5th East, Salt Lake* Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, 13-16. Mr. Ralph W. Neill, 1309 Seventh *Ave., Seattle 1,* Ex Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. L Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, land, Oct. 15-17. For information write: Dr. Bertram B. Moss, 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngolog Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, ond St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicag 5-8. *Dr. E. H. Christopherson, 1801 Hinman Ave.,* Evanston Executive Secretary.

American Association of Medical *Assistants, Benjamin* Franklin Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearb Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Ph phia, Oct. 23-25. Dr. *Philip* Reichert, *Empire State Bldg.,* New Executive Director.

American College of Chest Physicians, 25th Anniversary Hon ing Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Ko 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassad lantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Ph phia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., Ne 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Loui 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary

American Otorhinologic Society for Plastic Surgery, Inc., Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Detroit 24, Co-Chairman, *Planning Committee.*

American Public Health Association, Convention Hall, Atlanti N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hote *Harbour, Fla., Oct. 5-9. Mr. John W.* Andes, 188 W. Randolp Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray bent, 508 E. South Temple, Salt Lake City. General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Miami 33, Fla., Executive Secretary.

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OCULAR SURGERY IN THE AGED

Morris Feldstein, M.D., Abraham L. Kornzweig, M.D.
and
Julius Schneider, M.D., New York

The beneficial results of surgery were weighed against the risks in a review of 118 major eye operations on a series of patients from 65 to 94 years of age. Eighty-five operations were for cataract and 18 for glaucoma. Most patients had some form of circulatory disease, 19 had hernias, 16 had pulmonary emphysema, and 11 had diabetes. Nevertheless, there were only two deaths attributable to the operation. The declining years of many of these patients were immeasurably brightened by restoration of vision, which in some cases meant ability to carry on a reasonably self-sufficient and meaningful existence for many years without being a constant burden to others. Undue emphasis on the risks of operation can lead to the withholding of beneficial ocular surgery in the aged.

OLD AGE presents special problems in major ocular surgery. In order to bring the light of experience to bear on this question, we have reviewed the 118 major eye operations done on the residents of the Home for Aged and Infirm Hebrews of New York over the past 15 years. These persons were all over 65 years of age.

We have studied the types of operations, the preoperative medical status, age at operation, the results of surgery, and the complications which we have encountered, both local and general, and have tried to derive some general principles as to the feasibility of surgery and the risks involved in this age group.

Indications and Contraindications

The indications for ocular surgery were fairly limited in scope. Most of the operations were for restoration of vision which had been lost due to cataract formation. Surgery was also used in cases of glaucoma when medical measures had failed. There were other indications, but these were relatively few in number.

Table 1 lists the number of operations in the different categories. Cataract extractions total 85 cases, or 72%. Operations for glaucoma were done in 18 cases, and there were 4 operations for retinal detachment. The balance, as can be seen from the table, is composed of a small number of different procedures.

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The most important contraindication for performance of surgery was the presence of a psychotic state which rendered the patient unmanageable or likely to be unaware of his visual status. A second one was the patient's own lack of desire for surgery despite the presence of a material decrease in vision. However, in such cases if there was any condition likely to cause irreversible damage to the eye, such as the presence of glaucoma or a hypermature cataract, the patient was strongly urged to undergo surgery and usually he followed this advice. Occasionally there were situations where surgery would have been considered except for the presence of another condition which was an active threat to life itself. In such instances the elective surgery of the eye was either postponed or abandoned.

TABLE 1.—*Types of Ocular Surgery Performed on Persons over Sixty-five Years of Age in 118 Cases*

Cataract extraction	85
Intracapsular	68
Extracapsular	17
Discission	4
Glaucoma procedures*	18
Enucleation	2
Retinopexy	4
Dacryocystorhinostomy	1
Biopsy of lacrimal gland	1
Tarsorrhaphy	1
Sphincterotomy	1
Dacryocystectomy	1
Total	118

*See table 5.

However, numerous serious medical conditions which coexisted at the time surgery was indicated were considered as deterrents rather than absolute contraindications. These included coronary sclerosis with severe insufficiency, severe diabetes, status after recent myocardial infarction, status after recent cerebrovascular accident, advanced hypertension, and severe asthma. No attempt was made to set up hard and fast rules, since each problem was discussed and evaluated with the medical staff. The complicating conditions and their frequency are listed in table 2. Hypertension of varying degrees was by far the commonest condition encountered at the time of operation. Arteriosclerotic heart disease was present in many patients. Hernias of all types, pulmonary emphysema, peripheral arteriosclerosis, general arteriosclerosis, varicose veins, and hypertrophy of the prostate were also encountered.

Risks Versus Gains

There were limited goals in the operations performed, particularly those concerned with cataract or glaucoma. Each operation was a calculated risk in itself, and oftentimes, in questionable cases, the patient's demands for vision were the deciding factor. The following case is of particular interest in this regard.

An 83-year-old male had bilateral cataracts. However, the medical department was loath to give permission for surgery because he suffered from left-sided heart failure, pulmonary emphysema, hypertension, epidermoid (squamous cell) carcinoma of the vocal cord, chronic cholecystitis, and severe orthopnea, which presented a special problem since cataract operations are usually performed with the patient in the recumbent position. When the patient finally threatened to commit suicide if something were not done to restore his vision, the medical department reluctantly, with the consent of the psychiatric department, agreed to permit the patient to undergo ocular surgery. A combined intracapsular cataract extraction was done on the right eye. The patient was operated on in a semirecumbent position. He was allowed out of bed the day of the operation, being permitted to sit up in a wheel chair. The postoperative course was completely uneventful. His medical condition showed no deterioration as a result of surgery. Within four weeks the patient was fitted with glasses, and his resulting vision was 15/30 in the right eye. Although he lived for only eight months after the operation,

TABLE 2.—*Antecedent General Diseases of Patients Undergoing Eye Surgery*

	No. of Patients
Hypertension	62
Arteriosclerotic heart disease	37
General arteriosclerosis	14
Peripheral arteriosclerosis	16
Congestive heart failure	7
Myocardial infarction	4
Diabetes mellitus	11
Pulmonary emphysema	16
Status after cerebral accident	4
Hypertrophy of prostate	8
Osteoarthropathy	7
Deafness	7
Prostatectomy	4
Kyphoscoliosis	7
Healed pulmonary tuberculosis	4
Varicose veins	13
Hernias, all types	19
Diverticulosis, colon	3
Diverticulosis, esophagus	3
Fracture, hip	3
Subtotal gastrectomy	3
Status after brain concussion	3
Paralysis agitans	3
Hemorrhoids	6
Thrombophlebitis	2
Asthma	1
Pulmonary atelectasis	2
Epidermoid (squamous cell) carcinoma of vocal cord..	1
Syphilis	1
Amputation, leg	1
Senile schizophrenia	1

those months were immeasurably brightened by his ability to see. All members of our staff agreed that the risks taken in this case were thoroughly justified.

There were other cases with similar considerations in varying degrees. These older persons stand to gain a great deal by the restoration of vision in their declining years in spite of whatever risks may be entailed. This became more apparent as we realized that these risks have frequently been overestimated. It would be well indeed for physicians in general to approach this problem with a fresh viewpoint.

Age Distribution

Most of the operations were done on patients between 75 and 84 years of age (70 patients). The balance of cases was evenly distributed between those in the age groups 65-74 (28 patients) and 85-94 (20 patients). Operative indications were not encountered in anyone over 94 years of age.

Results

The results of the cataract extractions were extremely encouraging (table 3). In 59, or 87%, of 68 intracapsular cataract extractions there was vision of 15/70 or better as a result of operation. Of 17 extracapsular cataract extractions done, 12, or 71%, resulted in vision of 15/70 or better. When both types of procedures are considered together, a total of 71 eyes, or 84%, showed a vision of 15/70 or better. This is sufficient vision to enable the patient to take care of himself.

Table 3.—*Vision After Cataract Extraction in Eighty-five Cases*

Vision	Intracapsular	Extracapsular
15/20	3	...
15/25	8	1
15/30	14	4
15/40	18	6
15/50	8	1
15/70	8	...
15/100	2	...
15/200	7	5
	68	17
15/70 or better	59(87%)	12(71%)

Postoperative vision after cataract extraction is shown in table 4 according to age group. The majority of patients had vision of 15/70 or better in every one of the age groups. Detailed analysis of the cases in which vision was 15/200 or less revealed adequate reason for the poor vision; each patient showed pathological changes which could not be attributed to surgery, except for one case of severe vitreous hemorrhage. It is important to note that in these cases, with the exception of those of optic neuritis and vitreous hemorrhage, all patients had a return of useful peripheral vision after cataract extraction. Their central vision was defective by reason of their particular eye lesions. However, they were usually grateful for the peripheral vision that they obtained as a result of the operation. It is important to appreciate the full value of the vision provided by the retina outside of the macular area. Even though the macula is destroyed, the vision remaining in the rest of the field is sufficient to enable the person to carry on a reasonably self-sufficient and meaningful existence without being a burden to others around him. Therefore, even though visual acuity may be reduced by reason of macular damage, cataract extraction in this older age group is still definitely indicated when cataracts are present together with macular degeneration.

Table 4.—*Vision After Cataract Extraction, by Age Group*

Age Group	15/20	15/25	15/30	15/40	15/50	15/70	15/100	15/200 or Less
65-74		2	6	6	2	2	0	1*
75-84	2	6	10	13	5	6	1	10†
85-94	1	1	2	5	2	0	1	1‡

* Optic neuritis.

† Preoperative senile macular degeneration, 4; old glaucoma, 3; diabetes with macular degeneration, 2; and vitreous hemorrhage, 1.

‡ Diabetic retinitis.

The cases of glaucoma are listed in table 5 according to type of operation and result obtained. Most were controlled either with or without medication after surgery. Two cases were uncontrollable even after surgery and went on to total blindness. In general, we favor the use of iridencleisis and found it reasonably successful in the comparatively few cases of glaucoma that we treated. However, this experience is too small to justify any general conclusions.

Complications

The postoperative complications were few in number, especially in view of the age of our patients (table 6). The complications are divided into two types, general and ocular. In most of the cases there were no general complications. This is of particular interest because of the fears that attend any ocular surgery in this age group, not only in the minds of the patient's family but also in the mind of the attending physician. Many patients had the usual diseases found in this age group, in both number and severity, yet it was extremely gratifying to find that there were relatively few postoperative general complications. Of the 10 patients with general complications, 6 suffered from transient postoperative psychosis. In more recent experience this complication has largely been eliminated be-

Table 5.—*Results of Treatment of Glaucoma in Eighteen Patients*

		Controlled		
Type of Operation	No. of Cases	Without Medication	With Medication	Uncontrolled
Iridencleisis	11	3	8	...
Iridectomy	2	1	1	...
Corneoscleral trephination	2	...	1	1
Cyclodiathermy	3	...	2	1

At the time of this writing, four weeks after the anaphylactic reaction, the patient is up and about, his blood pressure and pulse rate are normal, and his cardiovascular findings are quite satisfactory. He remains disoriented as to time and place, and this is perhaps best explained by the cerebral injury due to anoxia during the severe cardiovascular collapse in an elderly arteriosclerotic person. There is no paralysis.

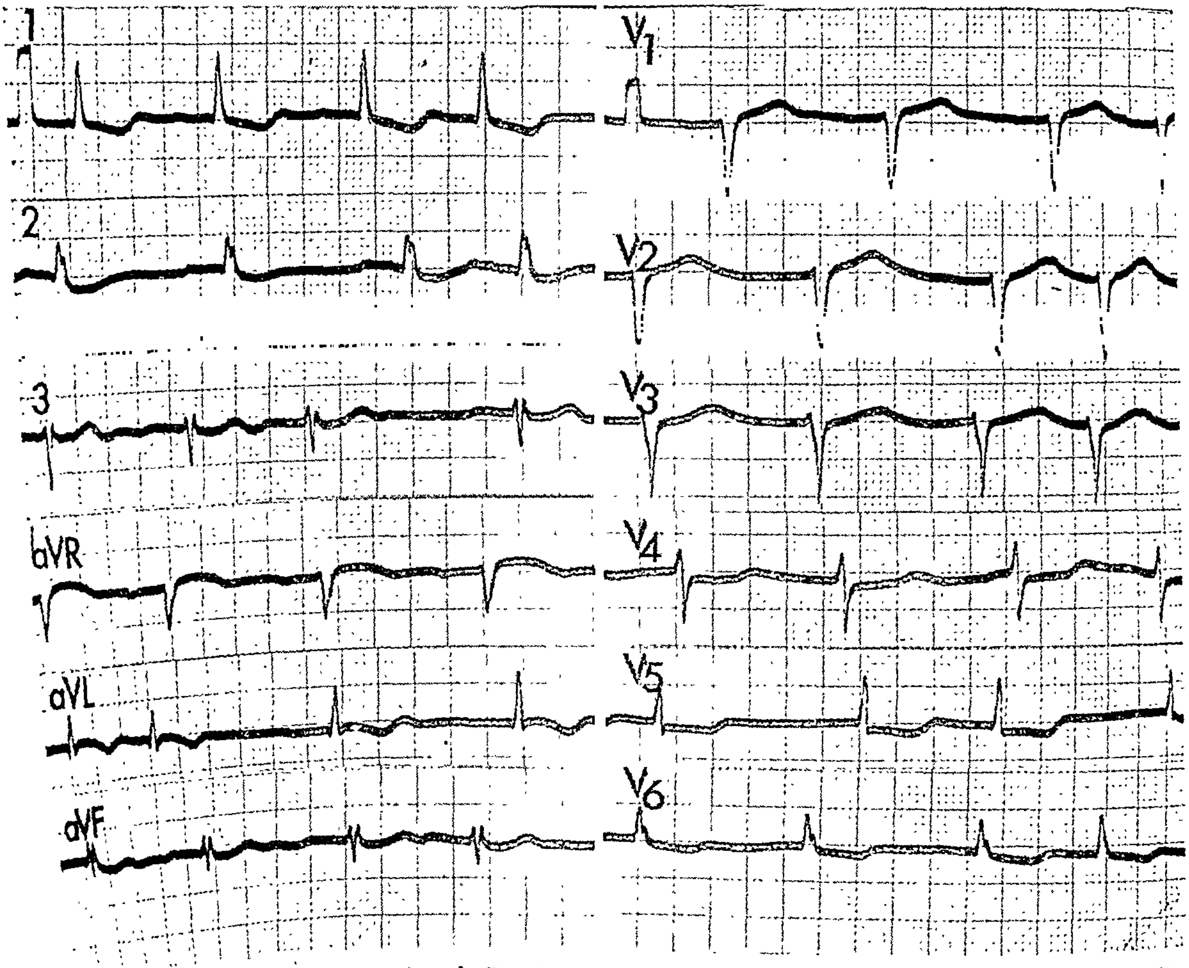

Fig. 2.—Electrocardiogram taken approximately 50 minutes after that in figure 1. Auricular fibrillation has changed to sinus mechanism, and occasional auricular premature contraction is present. The P-R interval is prolonged to 0.24 seconds. There is evidence of left ventricular strain and insufficient coronary circulation. Intraventricular conduction disturbance, as well as injury pattern, has disappeared.

Summary and

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SIMPLE BEDSIDE TEST OF RESPIRATORY FUNCTION

Thomas H. Snider, M.D., John P. Stevens, M.D., Freeman M. Wilner, M.D.
and
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The ability of a patient to blow out a match at a distance of 6 in. (15 cm.) was found to be a useful clinical test if conditions were duly standardized. This ability was tested in 126 patients and shown to be well correlated with the results of two other tests of respiratory function, namely, the tests for one-second vital capacity and maximum breathing capacity. The match test is feasible as a bedside procedure for detecting signs of airway obstruction. If it gives positive results, more specific tests for pulmonary function should be performed.

The bedside signs of obstruction to air flow, such as wheezes and prolonged expiration, do not give the quantitative information needed to properly evaluate respiratory function. Two quantitative tests for airway obstruction in common use today, determination of the maximum breathing capacity[1] and determination of the timed vital capacity,[2] require special equipment not available at the bedside. In this report a simple, semiquantitative, bedside test for airway obstruction is evaluated.

The inability to blow out a match held near the open mouth depends on the velocity of air flow and thus may be affected by airway obstruction. We have standardized this procedure and in this report correlate the ability to blow out a match with the maximum breathing capacity and with the one-second timed vital capacity in 126 patients with various forms of pulmonary disease.

Method

Standard book matches are used. After the initial flare, when the match is burning steadily, it is held 6 in. from the patient's open mouth. The patient is first instructed to inspire maximally and then expire rapidly in an attempt to extinguish the burning match. It is important that the patient not purse his lips, for he must expire with his mouth completely open to measure true air-flow velocity. This procedure is repeated several times to assure maximal effort on the part of the patient. All patients tested in this study performed the timed (one-second) vital capacity (with use of the Gaensler-Collins Vitalometer) and maximum breathing capacity[3] tests, and results of these tests were correlated with those of the match test.

Results

A total of 126 patients were tested. Seventy-four were able to extinguish the match, using the method described, while 52 could not. The mean value of the one-second vital capacity for those who could not blow out the match was 0.97 liter with a standard deviation of ± 0.47 liter. For those who could extinguish the match the mean value for the one-second vital capacity was 2.49 liters with a standard deviation of ± 0.57 liter. Eighty-five per cent of the 52 patients who could not blow out the match had a one-second vital capacity below 1.60 liters, while 85% of the 74 patients who could blow out the match had a one-second vital capacity greater than 1.60 liters.

The 52 who could not blow out the match had an average maximum breathing capacity of 40.7 liters per minute with a standard deviation of ± 16.53 liters per minute. The 74 who could blow out the match had an average maximum breathing capacity of 93.0 liters per minute with a standard deviation of ± 25.85 liters per minute. Eighty per cent of the 52 who could not blow out the match had a maximum breathing capacity below 60 liters per minute, while 80% of the 74 who could extinguish the match had a maximum breathing capacity above 60 liters per minute (fig. 1 and 2).

The match test appears to be a fairly reliable semiquantitative guide to airway obstruction. It may fail to differentiate, however, certain patients with a greatly reduced total vital capacity due to pulmonary fibrosis and other conditions limiting expansion of the lungs from patients with airway obstruction. This is because the one-second vital capacity may be a normal percentage of the reduced total vital capacity but still inadequate to extinguish the match. The normal patient with a total vital capacity of 4,000 cc. usually exhales at least 3,200 cc. of this in the first second and, since this exceeds 1,600 cc., is able to extinguish the match. The patient with obstructive emphysema with a total vital capacity of 3,000 cc. cannot blow out the match, for it takes him over one second to exhale 1,600 cc. Results in two patients with restrictive pulmonary disease due to pulmonary fibrosis

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cause only one eye is covered after operation. In previous years, when both eyes were usually covered after surgery, postoperative psychosis was more apt to occur. In this connection, it is worthwhile describing the following experience.

A 73-year-old female had only one functioning eye, and this eye had a mature cataract. A combined intracapsular cataract extraction was done and this one eye was dressed, leaving the patient in total darkness. The second day after operation she developed an acute postoperative psychosis. On the third postoperative day the patient was removed from the hospital and taken back to the Home. In addition, the dressing was removed and a plastic shield containing a +10 D. sphere in its center was placed over the eye and taped on securely. Underneath the shield, the eye was open. After transfer, the patient's psychotic condition began to improve, and in 48 hours she was again normal. The eye itself suffered no damage, healing uneventfully. Her final postoperative vision in this eye was 15/40.

TABLE 6.—*Postoperative Complications of Ocular Surgery in 118 Patients*

General	No.
No complications	108
Complications present	10
Myocardial infarction with recovery. Preexisting history of 1 occlusion and anginal syndrome for 2½ yr.	1
Acute postoperative psychoses	6
Pulmonary infarction	1
Death	2
Female, aged 75: postoperative congestive failure with death after 14 days	
Female, aged 83: acute myocardial infarction with death on 2nd day after operation	
Ocular	
No complications	106
Complications present	12
Mild iritis due to lens cortex in anterior chamber after cataract extraction. Recovered	
Postoperative cataract. Choroidal detachment after 8 days. Reattached spontaneously	
Extracapsular cataract extraction. Temporary postoperative glaucoma and iritis	
Postoperative cataract extraction. Iris prolapse. No further surgery. Result good	
Cataract extraction. Vitreous hemorrhage. Slow recovery over period of 3 yr.	
Cataract extraction. Postoperative glaucoma. Controlled with medication (2 patients)	
Cataract extraction. Vitreous loss during operation and postoperative hyphema. Eventual recovery of vision	
Cataract extraction. Postoperative hyphema. Absorbed quickly	
Cataract extraction. Postoperative retinal detachment. Operation successful for retinal detachment	
Cataract extraction. Postoperative corneal dystrophy. Eventual loss of vision	
Cataract extraction. Endophthalmitis. Eventual phthisis bulbi	

The two cases in which death occurred are worthy of special consideration. In one there had been a history of previous myocardial infarction and repeated bouts of cardiac failure over the preceding two years. However, the operation was performed because the patient was completely disabled by her cataracts and personally requested that cataract extraction be done. Death due to myocardial infarction occurred two days postoperatively. One can only wonder whether this death was due to the operation or might not have occurred anyway. The second case, in which congestive heart failure and death occurred 14 days after operation, raises the same question. Since people in this age group are continually suffering incidents of myocardial infarction, pulmonary infarctions, and other emergencies, an occasional complicating incident of such type may be expected to occur coincidentally with surgery. However, even if we attribute these unfortunate sequelae to the surgical intervention, they still constitute an extremely small percentage of the total.

The effect of hypertension requires special comment. This condition was present in 62 of the 118 patients operated on. In spite of this, the incidence of hemorrhage or other complications feared as a result of hypertension was extremely low. Only one vitreous hemorrhage was encountered and one hyphema. This actually is less than the usual percentage encountered in the average published series in younger persons. One should not be fearful, therefore, of hypertension when one is considering the feasibility of ocular surgery.

The ocular complications were few in number. There is a total of 12 such cases, and these are enumerated in table 6. One patient developed mild iritis, presumably due to the presence of lens cortex in the anterior chamber after cataract extraction. There was an uneventful recovery from this. Another patient suffered postoperative choroidal detachment; reattachment occurred spontaneously. Postoperative glaucoma and iritis turned out to be a temporary condition which resolved under medical treatment in one case. A case of postoperative iris prolapse after cataract extraction was merely observed. The patient continued to enjoy good vision and the condition of the eye remained quiet. The case in which vitreous hemorrhage was encountered was of particular interest. The patient's case was followed over a period of three years, during which time there was slow recovery of vision. Eventually vision was 15/40 with correction.

Two cases of glaucoma developing after cataract extraction were controlled with medicaments. Another patient in whom vitreous loss was encountered during operation and development of postoperative hyphema followed had poor vision for several years. However, eventually the vision became 15/50 in this eye with correction, which was a most unexpected result. Another case of cataract extraction with postoperative hyphema was followed by uneventful absorption of the hyphema. A patient with

600,000 units of penicillin the morning of the operation and within a few minutes experienced severe respiratory distress and quickly collapsed. Pulse and blood pressure became unobtainable five minutes after the administration of penicillin, and the patient appeared in extremis. At this time epinephrine, 1 cc., and hydrocortisone sodium succinate (Solu-cortef), 100 mg., were administered intravenously and levarterenol (Levophed), 4 cc. in 500 cc. of dextrose, was given as an intravenous drip.

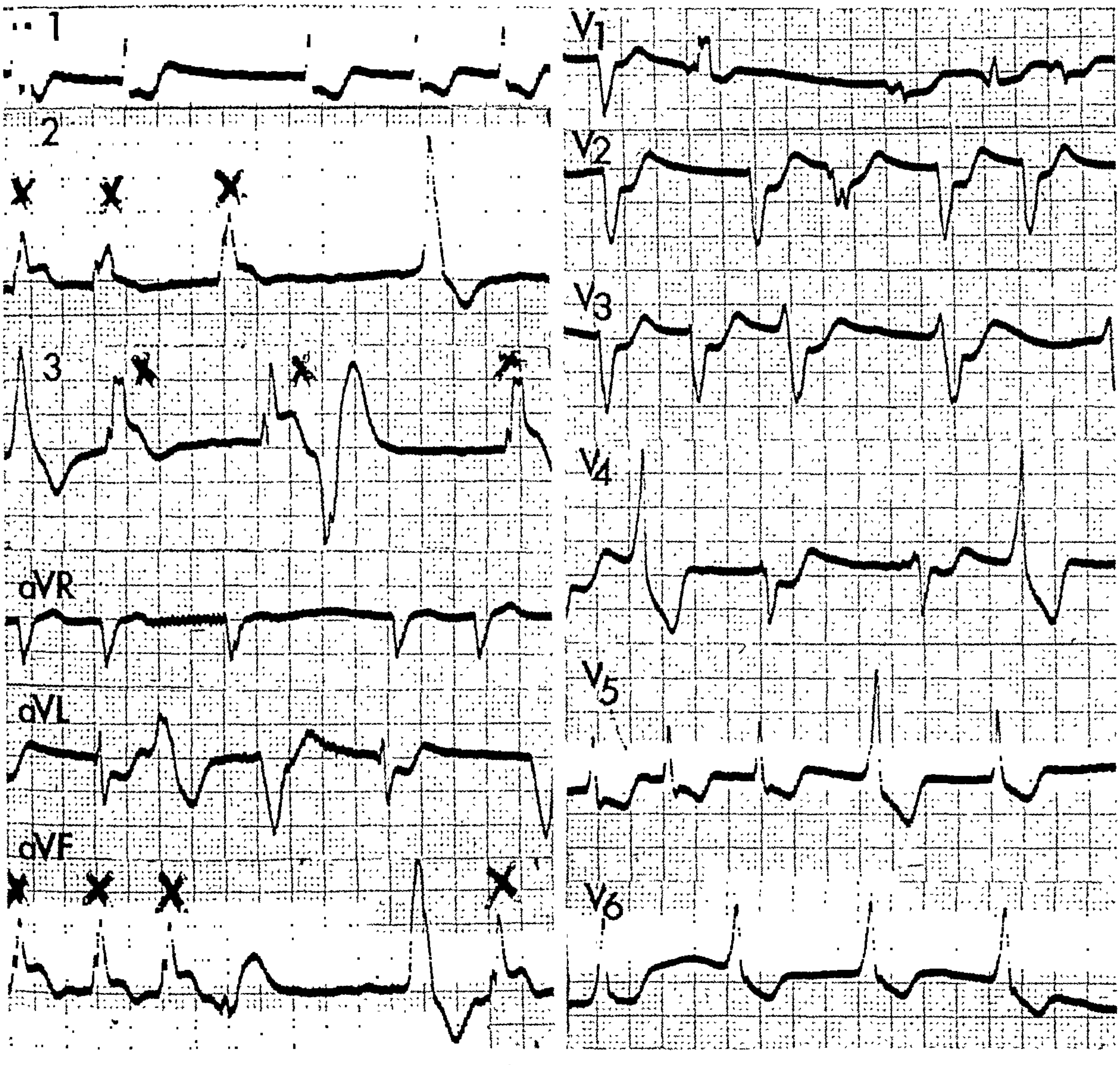

Fig. 1.—Electrocardiogram taken 15 minutes after administration of penicillin, showing auricular fibrillation, multifocal ventricular ectopic beats, and intraventricular conduction disturbance. Findings in leads 2, 3, and aVF (marked X) indicate severe coronary insufficiency and injury in posterior wall of left ventricle.

An electrocardiogram taken 15 minutes after the penicillin administration (fig. 1) and while the patient was in severe shock showed auricular fibrillation, intraventricular conduction disturbance, severe coronary insufficiency, and marked injury to the posterior wall of the left ventricle. A second electrocardiogram (fig. 2), taken approximately 50 minutes after the first, showed a remarkable change toward normal. The patient was regaining consciousness at that time, and a giant urticaria-like eruption became apparent over the entire body. From then on the patient made a complete recovery as far as his cardiovascular system was concerned. A third electrocardiogram was taken about three weeks later. This showed a regular sinus rhythm, with a slightly prolonged P-R interval, left ventricular strain, and insufficient coronary circulation. (No tracing before the occurrence of shock was available for comparison.)

At the time of this writing, four weeks after the anaphylactic reaction, the patient is up and about, his blood pressure and pulse rate are normal, and his cardiovascular findings are quite satisfactory. He remains disoriented as to time and place, and this is perhaps best explained by the cerebral injury due to anoxia during the severe cardiovascular collapse in an elderly arteriosclerotic person. There is no paralysis.

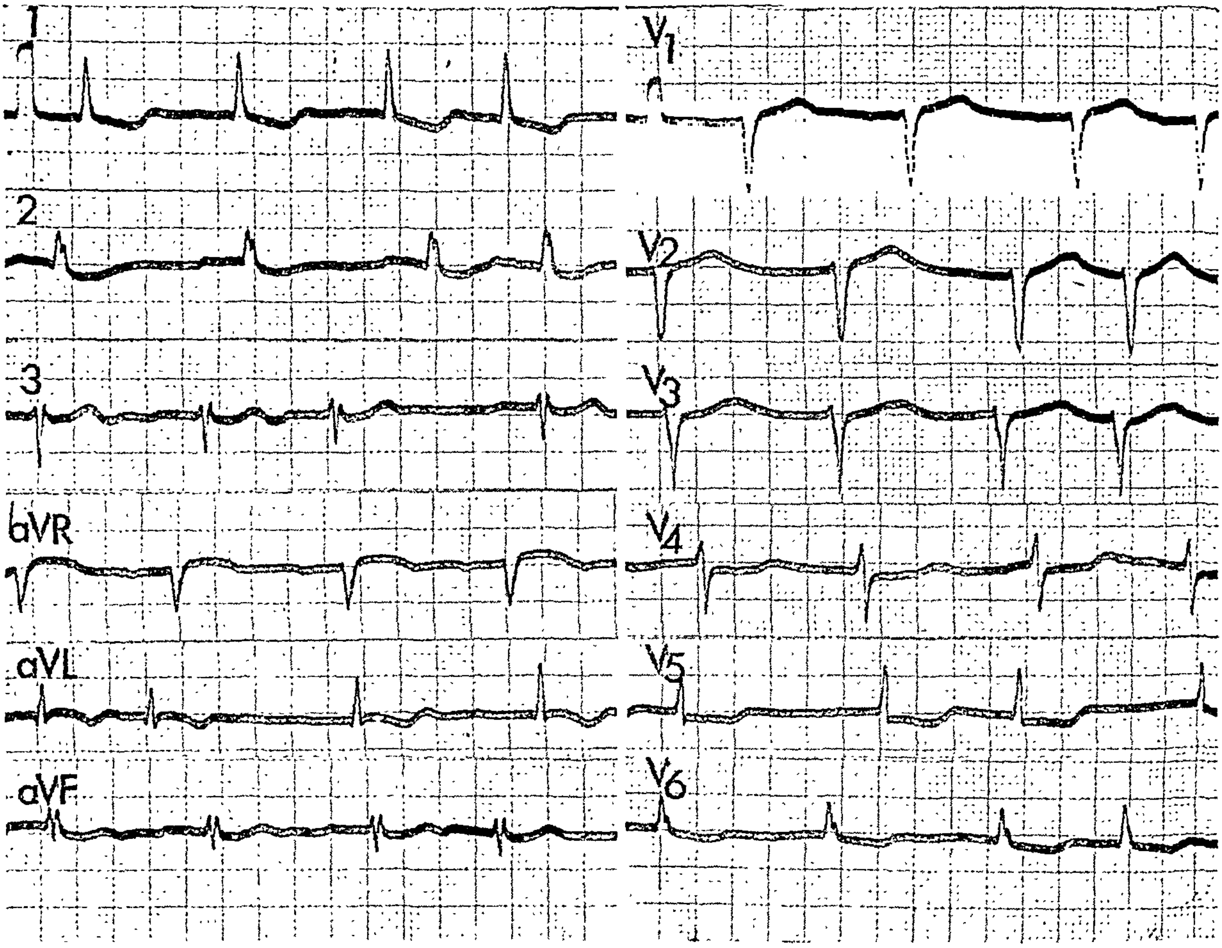

Fig. 2.—Electrocardiogram taken approximately 50 minutes after that in figure 1. Auricular fibrillation has changed to sinus mechanism, and occasional auricular premature contraction is present. The P-R interval is prolonged to 0.24 seconds. There is evidence of left ventricular strain and insufficient coronary circulation. Intraventricular conduction disturbance, as well as injury pattern, has disappeared.

Summary and Conclusion

A case of severe, nearly fatal, anaphylactic reaction to penicillin occurred in an elderly man. An electrocardiogram was taken at the height of the shock and approximately 50 minutes later. The severe electrocardiographic changes were transient. The patient made a complete recovery as far as his cardiovascular system was concerned, but the central nervous system showed less satisfactory recovery. The efficacy of the treatment in promptly reversing the electrocardiographic abnormalities strongly suggests that the myocardium and the coronary circulation are capable of participating directly in anaphylaxis and that sudden death during such reaction may be explained on this basis.

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Standard book matches are used. After the initial flare, when the match is burning steadily, it is held 6 in. from the patient's open mouth. The patient is first instructed to inspire maximally and then expire rapidly in an attempt to extinguish the burning match. *It is important that the patient not purse his* lips, for he must expire with his mouth completely open to measure true air-flow velocity. This procedure is repeated several times to assure maximal effort on the part of the patient. All patients tested in this study performed the timed (one-second) vital capacity (with use of the Gaensler-Collins Vitalometer) and maximum breathing capacity[3] tests, and results of these tests were correlated with those of the match test.

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are shown in figure 3 along with those of a normal subject and of a patient with pulmonary emphysema. Both patients with pulmonary fibrosis have low total vital capacities. However, one can exhale 1,600 cc. in the first second and can therefore blow out the match, while the other with a total vital capacity less than the required 1,600 cc. cannot blow out the match, even though neither has airway obstruction. Obviously, if the patient cannot extinguish the match more specific tests of pulmonary function should be performed.

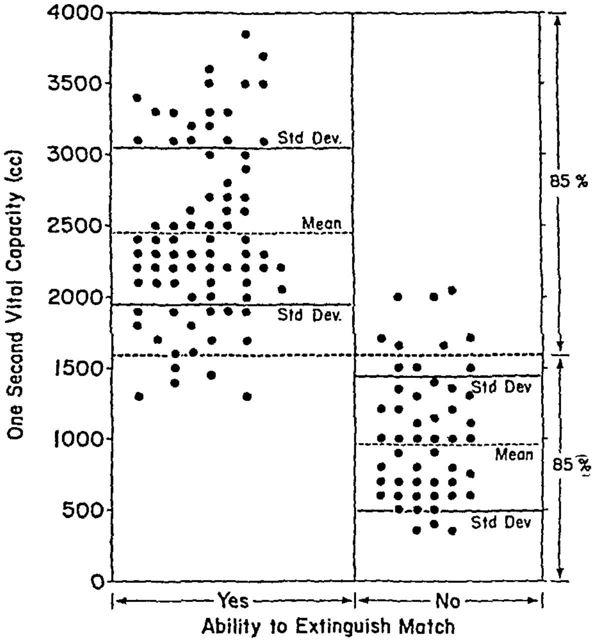

Fig. 1.—Results of one-second vital capacity match test.

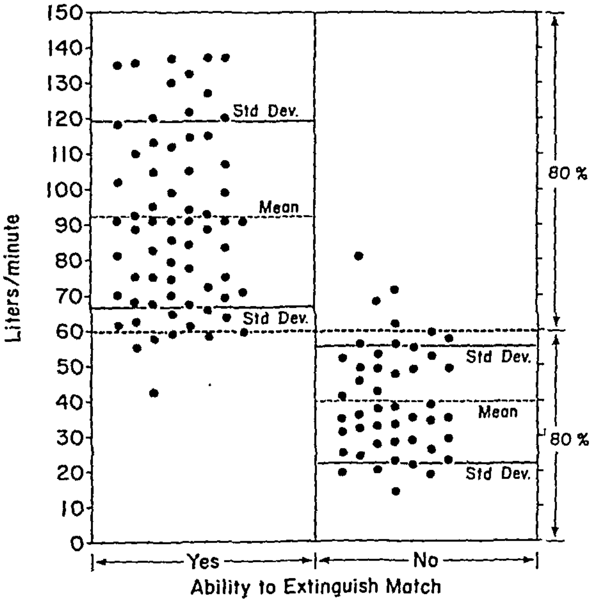

Fig. 2.—Maximum breathing capacity test results.

Summary

A simple semiquantitative test for airway obstruction is based on the patient's ability, by maximal expiration, to extinguish a match held 6 in. from the open mouth. Results of this test can be correlated with those of the one-second vital capacity and the maximum breathing capacity tests. Eighty per cent of the patients with a maximum breathing capacity above 60 liters per minute could extinguish the match, while 80% of those with a maximum breathing capacity below 60 liters per minute could not. Eighty-five per cent of those with a one-second vital capacity above 1.6 liters could extinguish the match, while 85% with a one-second vital capacity below 1.6 liters could not.

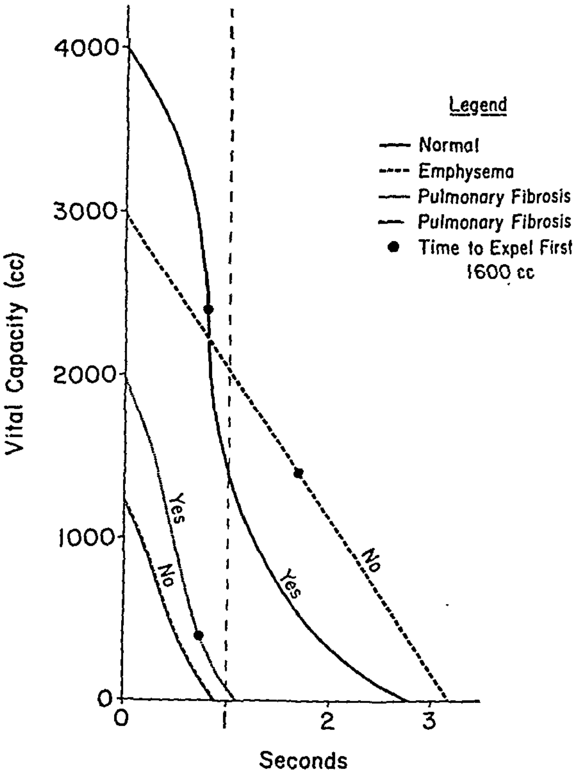

Fig. 3. Timed vital capacity in pulmonary disease.

Occasionally, patients with restrictive pulmonary disease will give results similar to those found in airway obstruction. Therefore, this test should be used only as a screening procedure; if results are abnormal, more specific tests of pulmonary function should be performed for exact diagnosis.

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CLINICAL EVALUATION OF SALINE SOLUTION THERAPY IN BURN SHOCK

II. COMPARISON OF PLASMA THERAPY WITH SALINE SOLUTION THERAPY

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In 79 burned adults, including 11 with burns of over 50%, treated with saline solution alone, there was no two-day mortality. In 74 other adults, including 14 with burns of over 50%, treated with plasma plus dextrose and water, there was a 12% two-day mortality. Selection of patients was made on a strictly alternating basis. In 73 burned children treated with saline solution alone, there was a 19% two-day mortality. In 92 other children treated with a combination of plasma and saline solution, there was only a 9% mortality. Saline solution therapy is considered good emergency therapy for adults, and addition of plasma to saline solution reduced the over-all acute mortality in children, particularly in the more severely burned.

This report of mortality and clinical data collected during the burn shock study in progress in Lima, Peru, is the second one of a series in which the efficacy of saline solution therapy is being evaluated. The administration of large quantities of saline solutions in burn shock stems from the experimental work summarized in a review by Rosenthal and Millican.[1] In the present study, the saline solutions for both oral and intravenous administration were isotonic saline solutions with electrolyte concentrations of sodium, chloride, and bicarbonate similar to those found in plasma of normal, healthy persons. The details of preparation are given in the earlier report.[2]

In the first report of this series,[2] one group of burned patients receiving only saline solution therapy in quantities roughly equivalent to 15% of body weight during the first 48-hour period after thermal trauma was compared on a strictly alternate case basis with another group receiving colloid (mostly plasma) supplemented by dextrose and water. Mortality during the shock period (48 hours) was used as the main criterion in evaluation of the efficacy of these therapies, since at the termination of the shock period there was no further difference in treatment of the two groups compared simultaneously. (The term "two-day mortality" is now being used in preference to 48-hour mortality, since the early mortality has been calculated in this paper, as it was in the first, to include all deaths up to 60 hours after burning.)

In adults, there was no mortality during the shock period in 40 patients treated with saline solutions as compared to a 10% early mortality in 43 patients treated with colloid supplemented by dextrose and water. The quantity of colloid administered was less than that recommended by Evans and co-workers[3] but represented the usual amount given to burned patients in Peru. Both groups showed a total mortality of 35%. Since the number of patients studied in each therapy group within each body-burn substratum was not sufficiently large at that time, it was not possible to conclude that the difference in two-day mortality was significant.

In a similar comparison of 110 burned children, there was no significant difference in two-day mortality between one group who received only saline solutions and the other group who received an adequate quantity of colloid supplemented by dextrose and water. The two-day mortality was 20% in both groups, with a 56% total mortality in the saline-treated patients as compared with a 62% total mortality in the colloid-treated patients.

In children, then, the mortality data demonstrated that adequate colloid therapy (mostly plasma) without adequate electrolyte therapy was not superior to treatment with saline solution alone. Since, however, most surgeons feel that treatment of burned patients with plasma is preferable to that with electrolytes alone,[4] the decision was made to investigate whether plasma combined with saline solution could significantly lower the early mortality below that seen with saline solution alone. This comparison was carried out in children, because (1) the results of the first therapy comparison in children were conclusive, while those in adults were not for lack of a large number of patients, and (2) since there was no (or very small) mortality from

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shock in the adult patients treated with saline solution it would not be possible to demonstrate an added benefit from plasma during the shock period.

For purposes of clarity this report is divided into two sections: series A, a continuation of the adult study as before with data presented now over a seven-year period and after an accumulation of 153 cases and, series B, a four-year study in 165 children comparing two groups receiving the same total amount of saline solution but with one group receiving as part of the therapy an adequate amount of plasma.

Series A—Methods and Materials

This report presents the results on the study of 153 severely burned adults (83 of whom were included in the first report) between the ages of 12 and 73 years. Ninety per cent of the burns were due to flames or fire, while the rest were due to hot fluids. The following types of cases were excluded from the study: (1) burns involving less than 10% of body surface area, (2) pulmonary burns, (3) burns in patients over the age of 73, (4) burns not treated within eight hours after burning, and (5) cases in which death occurred within two hours after treatment had begun. The patients were brought to the hospital from one-half to four hours after thermal injury had occurred, at which time they were placed, with strict alternation, into one of the two therapy groups, "saline" or "colloid."

The patients in the saline group received an average quantity of isotonic saline solution (given by oral or intravenous route exclusively or by a combination of the two) equivalent to 10% of body weight during the first day after thermal trauma and half that amount the second day. No additional liquid was administered either orally or intravenously. At no time was blood, plasma, or colloid given to these patients during this 48-hour period.

The patients in the colloid group with more than 25% of their surface area burned received in divided doses an average quantity of 0.43 ml. of plasma, blood, or povidone per kilogram of body weight for each percentage of area burned up to a 50% burn (averaging 1.7% of body weight) during the first 24 hours after injury and approximately half that amount (averaging 1.1% of body weight) during the second 24-hour period. All additional liquid in this group was given as water orally or as 5% dextrose in water intravenously. Of the 33 patients with 10 to 25% of their surface area burned, 21 received an average quantity of colloid equivalent to that received by those with more extensive burns, while 12 received only dextrose and water but no colloid therapy, due to an inadequate supply of colloid during the early part of the project. The patients who received only dextrose and water have been included in the colloid group for completeness of presentation, since their exclusion would not alter the final results, due to the fact that no two-day mortality occurred in adults with this degree of burn either in this or in the saline group (table 1).

Of the 62 patients receiving colloid, 52 (84%) received plasma or dehydrated normal human blood plasma (Lyovac) during the first 48 hours after burning in quantities of 0.2 to 1.2 ml. (average, 0.61 ml.; standard deviation, ± 0.19 ml.) per kilogram of body weight for each percentage of area burned; 6 (10%) received blood during the first 48 hours after thermal injury in quantities varying from 0.08 to 0.6 ml. per kilogram of body weight for each percentage of area burned; and 4 (6%) received povidone during this period in quantities varying from 0.6 to 1.3 ml. per kilogram of body weight for each percentage of area burned. The total amount of liquid (dextrose, water, and colloid) given during the first 48 hours after burning averaged 10% of body weight.

It must be emphasized that treatment of the two simultaneously compared groups differed only during the first 48 hours after injury. When patients had survived that period, there was no difference in therapy between the groups, since plasma and blood were given when necessary thereafter.

Blood pressure, pulse rate, respiration rate, and rectal temperature were recorded on admission, and, if the patient manifested signs of shock with a systolic blood pressure lower than 90 mm. Hg, intravenous therapy was started and followed by oral administration of fluid when the patient's blood pressure rose above 90 mm. Hg. In both therapy groups, half of the liquid administered during the first 24 hours after burning was given 8 to 12 hours after burning. The oral administration of the saline solution was accomplished simply by drinking of the liquid. If repeated vomiting or diarrhea occurred, oral administration of fluid was suspended and the intravenous route was utilized. The speed and quantity of fluid ingested were carefully controlled and recorded, and vomitus and urine were collected and accurately measured during this period when possible. Blood pressure, pulse rate, respiration rate, and temperature were measured every two hours during the first two days. Clinical notes were made every six hours.

All accessory antibiotic and supportive therapy was identical in both groups compared simultaneously.[2] Local therapy consisted of the open method for a period of nine days, after which the burned areas were covered with Vaseline-coated gauze and a heavier layer of dry gauze. Grafting was practiced initially within the first 18-28 days after burning in the majority of patients.

Series A—Results

As a consequence of strictly alternating cases between the two therapy groups, material was obtained in comparable groups with respect to the following pertinent variables: (1) percentage of body surface area burned, (2) percentage of body surface area with full-thickness burn, (3) causative agent, (4) age, (5) sex, and (6) interval between thermal injury and commencement of therapy. The resulting data, therefore, can be analyzed by overall groups or by subgroups wherever the total numbers are large enough to permit valid comparisons.

Table 1 gives the number of patients in each stratum of percentage body burn, two-day mortality, late mortality, and total mortality in each group, and 95% confidence limits on the percentage of two-day, late, and total mortality. In adults, there was no two-day mortality over a seven-year period in 79 patients (including 11 patients with burns over 50% of body surface area) treated with saline solution and a 12% two-day mortality in 74 patients (including 14 patients with burns over 50%) treated with colloid supplemented by dextrose and water. Of the nine patients in this group who died from shock, eight received plasma or dehydrated normal human blood plasma and one received blood as the administered colloid therapy. This difference in early mortality is statistically significant and demonstrates the superiority of treatment during the shock period with large volumes of saline solution over treatment with "inadequate" colloid supplemented with dextrose and water. In the late and total mortality, however, there is no significant difference between the two groups. It is noteworthy that patients in each substratum with burns over 25% of the body surface area showed a total mortality of over 50%.

Table 1.—*Mortality Data and Statistical Analysis in Burned Adults*

		Two-Day Mortality			Late Mortality			Total Mortality		
Burn, %	No. of Cases	No.	%	95% Confidence Limits, %*	No.	%	95% Confidence Limits, %*	No.	%	95% Confidence Limits, %*
Saline Group										
10-25...	38	0	0		3	8		3	8	0-17
26-50...	30	0	0		17	57		17	57	39-75
51-75...	8	0	0		7	88		7	88	
76-100..	3	0	0		3	100		3	100	
Total..	79	0	0		30	38	27-49	30	38	27-49
Colloid Group										
10-25...	33	0	0		2	6		2	6	0-14
26-50...	27	3	11	0-23	11	40		14	52	34-70
51-75...	9	2	22		7	100		9	100	
76-100..	5	4	80		1	100		5	100	
Total..	74	9	12	5-20	21	32	21-43	30	41	30-52

* 95% confidence limits connote that in repeated sampling 95% of the mortality percentages will fall between these limits. Any value that falls outside these limits is designated as significantly different. This statement will be expected to be incorrect with a probability of 1 in 20.

Percentage cumulative mortality in adults is plotted against time in figure 1*A*. The saline curve approaches the colloid curve only a fortnight after burning, and there is nothing to suggest that the administration of saline solutions caused an increase of mortality after the initial shock treatment period.

The routes by which the saline was given are listed in table 2. In burns of less than 50% of the body surface area in adults the majority of patients received the saline solution solely by the oral route, while more of the administered saline was given intravenously in the more serious burns, even though a fairly high percentage of these patients received some saline solution orally.

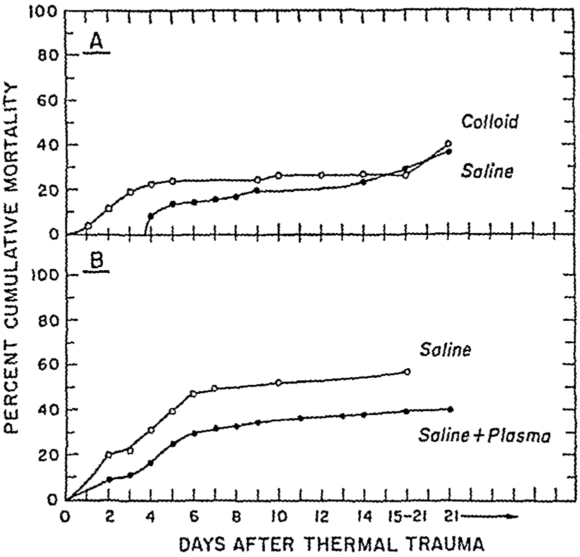

Fig. 1.—Cumulative mortality in burns over 10% or more of body surface area. *A*, adults; *B*, children.

Table 2.—*Mode of Saline Administration to Burned Patients*

		Oral		Intravenous		Combination		
Burns, %	No. of Cases	No.	%	No.	%	No.	%	Total Intake Given Orally in First 48 Hr., %
Series A, adults Saline Group*								
10- 25............	38	35	92	0	0	3	8	53
26- 50............	30	17	57	1	3	12	40	46
51- 75............	8	3	38	3	38	2	24	45
76-100............	3	1	33	1	33	1	34	7
Total..........	79	56	71	5	6	18	23	
Series B, children Saline Group*								
10- 20............	79	58	73	2	1	19	24	56
21- 30............	34	16	47	3	9	15	44	55
31- 40............	7	1	14	3	43	3	43	61
41-100............	11	0	0	5	45	6	55	27
Total..........	131	75	57	13	10	43	33	
Saline Plus Plasma Group								
10- 20............	54	44	83	3	6	6	11	43
21- 30............	22	6	28	9	41	7	30	39
31- 40............	9	3	33	2	22	4	45	29
41-100............	7	1	14	3	43	3	43	22
Total..........	92	54	59	17	18	20	23	

* Data for entire seven-year period.

Table 3 shows the incidence of toxic symptoms, including vomiting, diarrhea, and pulmonary edema, in adults and children treated over the seven-year period. In the adult patients who received only colloid supplemented with dextrose and water, the incidence of vomiting was significantly greater than in those who received saline solutions, while the incidence of diarrhea was slightly greater in the saline groups. It must be emphasized that no generalized and/or pulmonary edema was observed from clinical evidence or autopsy findings.

Table 3.—*Toxic Effects of Therapy During Shock Period*

Treatment Group	No. of Cases	Vomiting, %*	Diarrhea, %	Pulmonary Edema, %
Series A, adults				
Saline	79	16	9	0
Colloid	74	45	3	0
Series B, children				
Saline	73	14	12	0
Saline plus plasma	92	4	4	0

* Includes any vomiting after commencement of therapy.

As in the previous studies, an attempt has been made to evaluate therapy on the basis of its effect on clinical shock. Again blood pressure was selected as being, perhaps, the least subjective sign of shock. The incidence of hypotension in both therapy groups is illustrated in figure 2*B*. In general, the more extensive the burn, the greater was the incidence of hypotension at any time selected during the first 48-hour postburn period. In addition, the incidence of hypotension always increased for a minimum time of four hours after admission to the hospital, regardless of the therapy administered. In adults, both therapy groups showed a lower incidence of hypotension after fluid therapy had been administered than during the early course of the burn period, but the group that received inadequate colloid with dextrose and water demonstrated a higher incidence of hypotension at any time selected compared to the saline group.

Figure 3 illustrates the daily average urinary output with burns of increasing severity. In burns of 10 to 50% of the body surface area, where the number of patients studied was sufficiently large for statistical comparison, the 48-hour urinary output significantly ($p < 0.05$) decreased as the extension of the burn increased. The daily volume of urine was usually greater during the second 24-hour period after burning in both therapy groups. When the urinary volume was plotted as the percentage of ingested fluid excreted via the kidneys, the colloid group demonstrated a higher percentage of fluid excreted by the kidneys. Only the patients with 10 to 25% burns, however, showed a total 48-hour urine volume significantly different ($p < 0.05$) due to therapy.

Figure 4 demonstrates average weight changes over the initial weight and the percentage of fluid retained of the total amount of both adult groups. In burns up to 50% of the body surface area the patients in the saline group retained approximately 45% of the fluid administered during the first 24 hours after burning. This amount of fluid retained was 14% higher than that retained by a group of normal Peruvian persons given the same quantity of saline solution orally during the same time period.[5] Patients with extensive burns retained less fluid than those with moderate burns. Regardless of the severity of the burn, patients in the colloid group retained much less fluid than those in the saline group.

Series B—Methods and Materials

This study included 165 severely burned children between the ages of 2 months and 12 years. Sixty-one per cent of the burns were due to hot fluids, while the rest were due to flames or fire. Similar criteria for the exclusion of patients from the study were adopted as for adults. If the burn involved 10% or more of the body surface area, the patient was placed in one of the two therapy groups, "saline" or "saline plus plasma," with patients strictly alternated between these groups. The composition of the saline solutions administered was the same as of those given to adults.

The children in both the saline and saline plus plasma groups received a total amount of saline solution or saline solution plus plasma equivalent to 10% of body weight during the first 24 hours after burning and 5% of body weight during the second 24-hour period. Children in the saline plus plasma group, however, received as part of the total amount of fluid administered a quantity of plasma equal to 1 ml. of plasma or dehydrated normal human blood plasma per kilogram of body weight for each per-

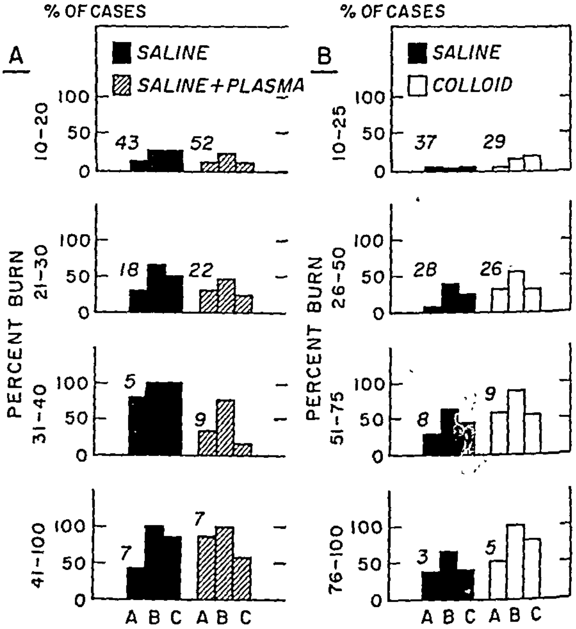

Fig. 2.—Incidence of hypotension in burned patients with systolic blood pressure below 90 mm. Hg. *A*, children; *B*, adults. Columns (*left to right*) represent admission, first 48-hour period after burning for minimum period of four hours, and end of 48 hours. Numbers above bars represent number of cases studied in each group.

centage of area burned, up to a maximum of 50% of the surface area burned (averaging 2.1% of body weight), during the first 24 hours after burning and half that amount in the second 24-hour period. The plasma was administered in divided doses, and the total quantity given was calculated from the formula of Evans and associates.[3] At no time during the first 48-hour period after thermal injury was any other type of fluid administered.

After 48 hours, there was no difference in therapy between the two groups. The clinical management was similar to that of adults. Infants were given fluid orally by constant drip technique with a tube passed through the nose to the stomach, whereas children over 2 years of age drank the saline solution. The criteria for giving the saline solution intravenously were the same as for adults.

Antibiotic therapy consisted of tetracycline in doses of 10 mg. per kilogram of body weight combined with polymyxin in doses of 2.5 mg. per kilogram of body weight. Because of the serious problem of Pseudomonas infection and septicemia as a major cause of late mortality,[6] a clinical evaluation of human gamma globulin was started during the last year and a half on the basis of the good results obtained with gamma globulin in the treatment of experimentally induced infections in mice.[7] Gamma globulin was administered intramuscularly on an alternate case basis in doses of 1 ml. per kilogram of body weight on the first, third, and sixth postburn days. The details of the gamma globulin study, which is under the direction of Dr. N. A. Kefalides, will be published later.

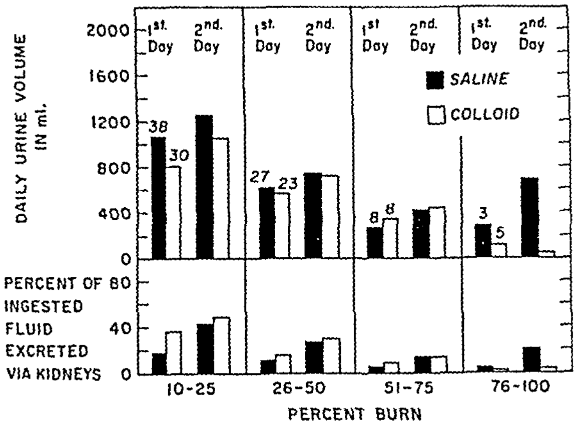

Fig. 3.—Average daily urinary output in burned adults (only patients in whom accurate urine collections could be accomplished are included). Numbers above bars represent number of cases studied in each group.

Accessory supportive therapy was the same as that previously described,[2] except that none of these children received desoxycorticosterone acetate. Local therapy consisted of washing the burned area with soap and saline solution, applying Prontyl (5.0 Gm. of azosulfanilamide, 0.05 Gm. of tetracaine, 12.5 Gm. of a solution of colloidal gelatin, and 100 ml. of distilled water) or an antiseptic to the wound, and covering the burn with Vaseline-coated gauze and dry gauze. Grafting was practiced initially within the first 18-28 days after burning in the majority of all patients.

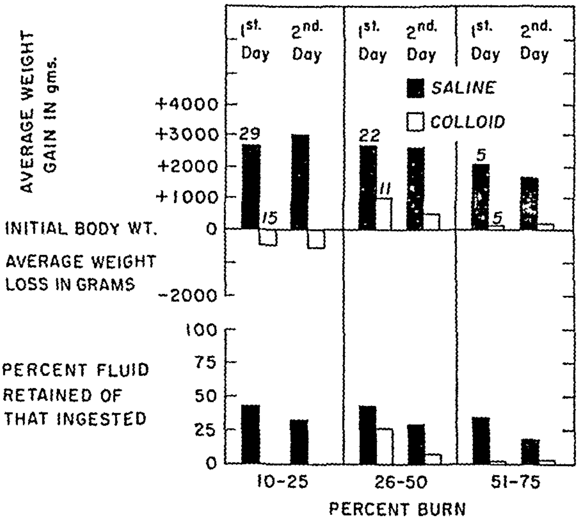

Fig. 4.—Average body weight change in burned adults. Numbers above bars represent number of cases used in computation of mean.

Series B—Results

The two-day mortality, late mortality, and total mortality are given in table 4 along with the 95% confidence limits. Again, as a consequence of strictly alternating the cases for treatment, material was obtained in comparable groups with respect to the same pertinent variables listed in the adult study. In children, there was a 19% two-day mortality in 73 patients treated with saline solutions and a 9% two-day mortality in 92 patients treated with ade-

Table 4.—*Mortality Data and Statistical Analysis in Burned Children*

		Two-Day Mortality			Late Mortality			Total Mortality		
Burn, %	No. of Cases	No.	%	95% Confidence Limits, %*	No.	%	95% Confidence Limits, %*	No.	%	95% Confidence Limits, %*
Saline Group										
10- 20..	43	2	5	0-12	17	41	26-56	19	44	29-59
21- 30..	18	4	22	2-42	7	50		11	61	39-83
31- 40..	5	3	60		2	100		5	100	
41-100..	7	5	71		2	100		7	100	
Total..	73	14	19	10-28	28	47	31-60	42	58	46-68
Saline Plus Plasma Group										
10- 20..	54	2	4	0- 9	8	15	5-25	10	19	9-29
21- 30..	22	2	9	0-21	11	55		13	59	37-81
31- 40..	9	1	11		6	75		7	78	
41-100..	7	3	43		4	100		7	100	
Total..	92	8	9	3-15	29	35	25-45	37	40	30-50

*95% confidence limits connote that in repeated sampling 95% of the mortality percentages will fall between these limits. Any value that falls outside these limits is designated as significantly different. This statement will be expected to be incorrect with a probability of 1 in 20.

quate plasma and saline. (The reason for the unequal numbers in these two groups is due to the fact that at the commencement of the project a strict alternation was used of two saline plus plasma cases for every one saline case, but after a year this plan was changed to alternation of single cases.) The over-all difference in early mortality is statistically significant and demonstrates that plasma combined with saline solution, as compared with saline solution alone, does improve survival, at least in children in Peru.

In the subgroup of 10 to 20% burns, the late mortality was significantly lowered by saline plus plasma therapy ($p < 0.05$), while the over-all late mortality showed no difference of statistical significance. The beneficial effect of plasma combined with saline solution was not only evident, therefore, in increasing survival during shock but also in decreasing late mortality in the 10-20% burns. The total mortality, nevertheless, remains high (over 59%) in burns of over 20% of body surface area regardless of initial therapy during the shock period.

Table 5.—*Influence of Age on Early and Late Mortality in Burned Children*

	Saline Solution Therapy						Saline Plus Plasma Therapy					
	10-30% Burn			31-100% Burn			10-30% Burn			31-100% Burn		
		Mortality, %			Mortality, %			Mortality, %			Mortality, %	
Age Group, Yr.	No. of Cases	2-Day	Late	No. of Cases	2-Day	Late	No. of Cases	2-Day	Late	No. of Cases	2-Day	Late
0-2.9	30	14	60	6	67	33	37	5	35	5	40	60
3-5.9	14	7	21	2	100	...	29	7	17	5	20	60
6-8.9	13	0	23	1	0	100	9	0	11	2	50	50
9-12	4	25	0	3	67	33	1	0	0	4	0	75
Total	61	10	40	12	67	33	76	5	25	16	25	62

Percentage of cumulative mortality is shown in figure 1*B*. These curves demonstrate that in the third to seventh postburn days a 9% increase in mortality above the difference at the end of two days was reached by the saline group as compared to the saline plus plasma group, after which time there was no appreciable change in mortality difference between the two groups.

Table 5 shows that 47% of the total number of children treated were infants below 3 years of age. Both immediate and late mortality varied inversely with age in both therapy groups in burns of 10 to 30% of the body surface area, where the number of patients was sufficiently large to detect this trend. The table also shows that plasma added to saline therapy decreased acute and late mortality only in infants below 3 years of age in the 10-30% burn group. There was no significant increase in survival of children over 3 years of age treated with plasma. In the severe burns of more than 30% of the body surface area, however, plasma significantly decreased over-all immediate mortality.

The routes by which the saline solution was given to children are listed in table 2. In burns of less than 30% of the body surface area, the majority of patients receive the saline solution solely by the oral route, while with the more serious burns more of the administered saline solution was given intravenously, even though a fairly high percentage of these patients received some saline solution orally. Data have also been listed for the saline plus plasma group to demonstrate that there was no significant difference in the manner by which the saline solution was administered to account for the difference in mortality between the two therapy groups in children.

Table 3 shows that the incidence of vomiting and diarrhea was low in both groups with even fewer untoward effects observed in the group who received adequate plasma and saline. The data of the saline group presented here compared with that in the earlier publication[2] show a 50% decrease in the incidence of both vomiting and diarrhea during the past four years. This difference may be due to the experience gained in the more regularly spaced oral administration of saline solution and to the strict limitation of saline solution intake to 15% of body weight. Again there was no evidence of generalized or pulmonary edema.

The incidence of hypotension in both therapy comparisons is illustrated in figure 2*A*. In general, the more extensive the burn, the greater was the incidence of hypotension. The saline plus plasma group demonstrated a much lower incidence of hypotension at the termination of 48 hours than the group that received saline solution alone.

Comment

The two-day mortality data in adults demonstrate that a quantity of isotonic saline solution that is equivalent to 15% of the body weight is good therapy during the shock period, since there was no 60-hour mortality, even among 11 patients with burns of more than 50% of the body surface area. On the other hand, in the plasma plus dextrose group the over-all early mortality was 12%, while in 41 patients with greater than 25% surface area involvement it was 22%. The less favorable response in this group may be attributed to inadequate electrolyte therapy as well as inadequate plasma therapy. The fact remains, nevertheless, that therapy with adequate amounts of plasma could not improve on the zero mortality in the saline-treated patients, although it is possible that plasma given during the shock period might decrease late mortality. Whatever the arguments may be for the ideal therapy, we believe that all will agree that saline solution is good emergency therapy.

On the other hand, children treated with saline solutions demonstrated a 19-20% two-day mortality during two separate therapy comparisons. Why, then, was saline solution therapy more efficacious in adults than in children? The large number of infants below 3 years of age in whom early mortality was higher than that of the older children may have been responsible for this difference. The high early mortality may also have been related to the frequency of malnutrition in Peruvian infants.[8] The addition of plasma to saline solution therapy, at any rate, effectively reduced the overall acute mortality in children.

The influence of age on mortality was even more striking in late deaths. The high late mortality may have been related to the known susceptibility of infants to infection. Indeed, a large percentage of late deaths in infants was found to be associated with a Pseudomonas septicemia.[6] Plasma therapy may have reduced the late mortality in infants by the antibodies it supplied.

The question arises again as to whether these data from Peru are applicable in other parts of the world. Although no controlled comparison similar to the one in Peru has been made, Fox,[9] Moyer,[10] and Griswold [11] have reported success in the treatment of burned patients with the administration of large amounts of saline solutions during the early postburn period. Since there is no reason to believe that the mechanism of shock and the principles of replacement therapy are different in other parts of the world, even though differences in susceptibility may exist, there is every reason to expect similar results in other localities.

Summary and Conclusions

A study was made of 165 children and 153 adults from Peru suffering from burns that involved 10% or more of the body surface area. In burned children, treatment was strictly alternated between two groups receiving the same total amount of saline solution (15% of body weight) during the first 48-hour period after burning, but with one group receiving as part of its saline solution therapy an adequate amount of plasma (3.1% of body weight). In burned adults, treatment was strictly alternated between one group receiving a quantity of isotonic saline solution that was equivalent to 15% of body weight in the first 48-hour postburn period and another group receiving a quantity of colloid (mostly plasma), averaging 2.2% of body weight, supplemented by a quantity of dextrose and water equivalent to 7.8% of body weight.

The saline solution was administered almost exclusively by the oral route in burns of less than 50% in adults and less than 30% in children; nevertheless, even in the patients with more severe burns in both age groups a fairly high percentage of the saline solution administered was given orally. In general, saline solution was received by the patients without difficulty, and there was no serious evidence of toxic effects, such as persistent vomiting or diarrhea, generalized edema, or pulmonary edema.

There was no two-day mortality in 79 burned adults (including 11 with burns of over 50%) treated with saline solution alone, while there was a 12% two-day mortality in 74 burned adults (including 14 with burns of over 50%) treated with inadequate colloid supplemented with dextrose and water. This difference in two-day mortality was statistically significant. The late and total mortality, while fairly high, showed no difference of major significance.

In 73 burned children treated with saline solutions alone there was a 19% two-day mortality, while in 92 children treated with adequate plasma and saline solution there was only a 9% early mortality. This difference in early mortality showed statistical significance. The late mortality in the children with 10 to 20% burns was significantly lower in the saline plus plasma group, but the overall late mortality showed no difference of statistical significance between the two groups.

The two therapy comparisons reported here, in addition to a previous study comparing saline solution alone with adequate colloid and dextrose and water, furnish sufficient evidence to make the following conclusions: 1. In burned adults, isotonic saline solution given in quantities of 15% of body weight is effective therapy in preventing early deaths due to shock, since there was no mortality during the shock period in 79 burned adults. 2. In Peruvian children and infants, adequate plasma therapy combined with adequate amounts of saline solution is more effective than saline solution alone or adequate colloid and water alone in reducing early mortality. The effect of plasma in reducing early mortality was most prominent in the treatment of severe burns of more than 30% of the body surface area, whereas in the less severe burns the additive effect of plasma in decreasing early as well as late mortality was limited to infants below 3 years of age.

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Drs. I. S. Ravdin, Carl Moyer, and Jonathan Rhoads aided in formulating the procedures used. This work was carried out as a clinical extension of the findings of Drs.

Rosenthal, Tabor, and Millican in experimental animals and was conducted under the general supervision of Dr. Sanford M. Rosenthal.

Mr. Jacob Lieberman, National Institutes of Health, aided in statistical aspects of this study. Dr. Alberto Hurtado furnished laboratory space in the Departamento de Fisiopatología; Drs. Gilberto Morey and Carlos Martinez furnished facilities in the Hospital del Niño; and Drs. Belizario Sanchez and Fortunato Quesada furnished facilities in the Hospital Loayza and Hospital Dos de Mayo respectively.

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THE MECHANICS OF COMMON FOOTBALL INJURIES

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Classifying the injuries incurred by football players has given valuable clues for prevention, diagnosis, and treatment. The upper extremity is less liable to injury than the lower because usually it bears little weight and is not fixed, but certain typical injuries to it do occur and are here analyzed. The lower extremity is usually fixed by contact with the ground and burdened by the weight of the rest of the body; injuries to the pelvis and lower extremity are therefore more frequent and severe. The head and vertebral column have rightly received more attention than other body segments because of the frequency of damage to the face and the seriousness of damage to the brain and spinal cord. Here probably the most lethal weapon in football is the oncoming knee, which exerts forces that must either be absorbed by the head or transmitted to the vertebral column. It may be necessary to redesign some of the protective equipment now in use, including the present-day facial protection bars.

It is the basic premise of this paper that football presents certain inescapable injury hazards, due to the very nature of this vigorous body-contact sport, and that a knowledge of the mechanics of these injuries is essential to adequate medical history and definitive diagnosis. It is not the purpose to discuss preventive measures, such as preparticipation physical examination, proper training and conditioning, thorough knowledge of game techniques, and proper use of protective equipment. Nor is the objective to discuss the proper classification of participants into different categories according to age, weight, coordination, and physiological and mental maturity. The manner in which injury may be incurred and the injuries most likely to occur in a given situation will be discussed. This subject has received only scant attention by the medical profession at large, but a small corps of active observers—the team physicians, the coaches, and the trainers—has long recognized the constantly recurring pattern of situations from which injuries are likely to arise. To minimize these situations they have developed rules and regulations, encouraged research and development of protective equipment (fig. 1), and altered coaching methods for the protection of the player.

From the Orthopaedic and Fracture Clinic.

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Be this as it may, injuries will occur and the value of an appreciation of injury mechanics under normal playing and practice conditions cannot be overestimated. It is fundamental that the early detection and prompt diagnosis and evaluation of injury is essential to the successful treatment of athletic trauma. Diagnosis can usually be made most accurately in the first few minutes after injury, prior to the onset of swelling and protective muscle spasm. Unfortunately, the physician seldom sees the player until hours or days after he has been injured. The well-trained player moves automatically, depending on training, instinct, and conditioning, and his attention is directed toward the constantly unfolding pattern of play rather than his position, posture, balance, speed, and mode of body contact. It is more than likely that he cannot give an accurate history until his memory is refreshed by the probing questions of a physician familiar with the type of injuries likely to occur and the mechanics of those injuries.

In this discussion, I will outline the mechanics of some of the more common injuries which are unique to the game and attempt to translate the "locker-room" slang for these injuries into medical terminology.

The Upper Extremity

The shoulder complex actually consists of four joints which, through coordinated interplay, place the arm in the many positions required in daily use. Of these, the sternoclavicular and scapulothoracic joints are rarely injured in football, and it is with the acromioclavicular and shoulder joints that the physician is primarily concerned. By nature these joints have little inherent mechanical stability but depend on ligamentous strength and muscle balance for their integrity. The glenoid fossa forms a shallow socket for the reception of the humeral head and articulates with only a small portion of its cartilaginous surface at any time. The articulation between the acromion and clavicle is of fingernail size, yet it represents the articular-osseous connection between arm and trunk. Variations in the shape of the joint lead to further instability: the joint may be smaller than normal in size, may be slanting rather than at right angles at the face of the joint, or may be set with the clavicle riding high at the acromial junction. The majority of injuries to these two joints result from contact with other players (63%), although contact of the shoulder with the ground forms an appreciable group (30%) and there are a few miscellaneous causes of injury.[1]

The types of injury, in order of frequency, are contusions of the shoulder, acromioclavicular joint injury, shoulder muscle strains, sprains and dislocations of the shoulder, fractures of the clavicle, and other miscellaneous traumatic conditions.[2] In athletic parlance,[3] the "shoulder pointer" means contusion of the acromion and adjacent deltoid at the "point" of the shoulder. "Shoulder separation" applies to sprains, subluxations, and dislocations of the acromioclavicular joint. "Shoulder strain" designates actual strain of the internal rotator cuff by direct pull, contusions of the rotator cuff by indirect force impinging it between the humeral head and acromion, and sprains and subluxation of the posterior aspect of the shoulder joint. "Dislocation" of the shoulder applies to anterior and inferior capsular involvement with subluxation or dislocation. "Shoulder nerve injury" is a syndrome characterized by pain and swelling of the deltoid, numbness of the hand of about five minutes' duration, followed by weakness in abduction lasting for about two weeks; it is due to contusion of the deltoid in combination with a mild traction injury to the brachial plexus or direct injury to the axillary nerve in the quadrilateral space. "Knocked-down shoulder" is the term applied to the protective position assumed after musculotendinous injury to the shoulder-neck interval and usually involves local muscle spasm of the trapezius, rhomboid, and cervical erector spinae muscles, accompanied by acute unilateral pain. The term "glass arm" does not apply to football since it is not primarily a throwing sport. Let us now look more specifically at the various mechanisms of injury.

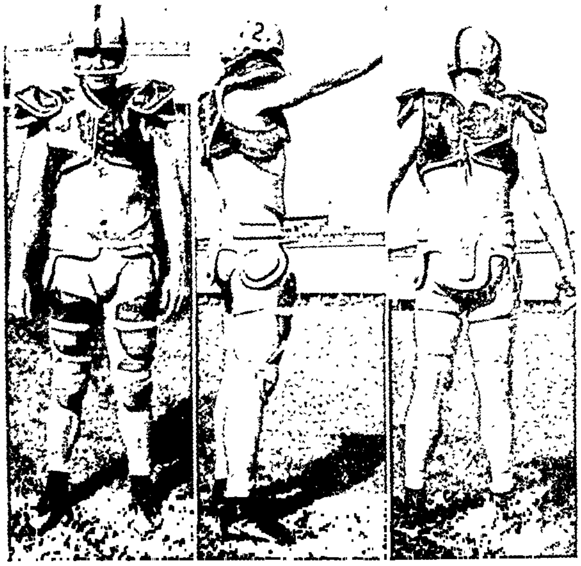

Fig. 1.—Football protective equipment. *Front view*, note headgear with bar protecting face. Within headgear is suspension, to distribute force of blow, with ⅝ in. clearance between scalp and shell. "Line-backer" shoulder pads distribute blow to shoulder area and thorax. *Side view*, note protection to roof of shoulder and deltoid region by shoulder pads. *Back view*, note protection to lower part of back and sacrum.

Mechanisms of Injury to Upper Extremity

The contusion of bone, muscle, or nerve is due to a direct blow. The roof of the shoulder and the shoulder-neck area are fairly well protected from such a blow by shoulder pads as long as these pads are properly sized and adjusted (fig. 1, *side view*). Only the trapezius and lateral part of the neck are exposed, and injury to this area most often occurs when the defensive player flinches and looks away from his opponent, taking a direct blow from the oncoming player's hip, thigh, knee, or elbow (fig. 2*A*). Trapezius injury may be incurred either from a direct contusion or sudden strong jerk on the arm while the head is being forced and rotated to the opposite side in a "pile-up" situation. Contusion of the brachial plexus usually results either from direct injury by the oncoming knee or thigh or from a downward blow on the shoulder resulting in impingement of the plexus between clavicle and ribs. Quadrilateral space injury is rare and is caused by a kick or blow from the knee. Contusion is usually of only transient importance since recovery time is seldom prolonged. Physical therapy methods are the chief form of treatment.

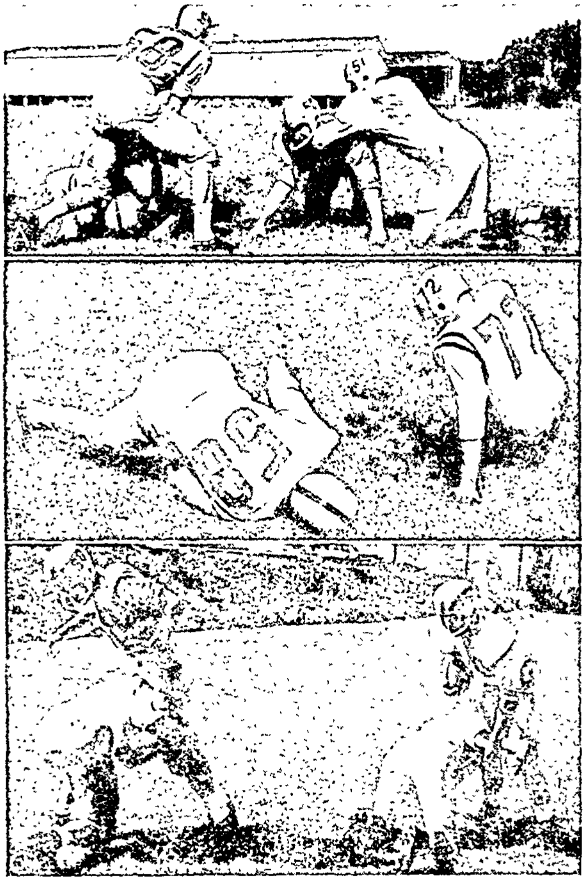

Fig. 2.—Injuries to shoulder-neck area. *A*, neck injury: defensive player exposes neck to block by dropping his head and failing to lift, probably due to flinching and closing eyes before moment of impact. He is likely to receive contusions of trapezius, cervical spine, and joint sprain. On right, player 50 looks away from defensive block, likely to cause head, neck, or facial injury. *B*, shoulder injury: player 58 is falling on "point" of shoulder, exposing himself to possibility of contusion of deltoid muscle and acromion, fracture of clavicle, and acromioclavicular sprain or dislocation. On right, player 72 has fallen with his arm at his side, exposing him to injuries of the wrist, elbow, and shoulder. *C*, two phases of mechanism of anterior dislocation of shoulder. On left, defending player tackles low and wide as ball carrier goes past. On right, his arm is being forced into abduction, extension, and external rotation.

Fractures of the clavicle are most often due to falls on the outstretched hand in which the force is transmitted upward through the shoulder and acromioclavicular joints to the clavicle. A lesser number are due to a fall on the point of the shoulder with inward force being carried through to the clavicle (fig. 2*B*). Fracture through direct injury is most rare because of the protective equipment, and for this reason fractures of the clavicle involving the underlying brachial plexus and subclavian vessels are seldom seen. It is obvious that most clavicular fractures are due to the failure of the player to absorb proper coaching techniques; in this case he fails to keep the body under control and to consummate a "body roll," in which the force of the blow is diffused by rolling backward over the posterior thorax and then into a prone position or onto the feet.[4]

The acromioclavicular articulation is subject to sprain, subluxation, or dislocation, all of which are due to essentially the same mechanics and are a matter of degree. Theoretically, this joint may be dislocated superiorly, anteriorly, posteriorly, or inferiorly. In football only the superior and anterior dislocations are seen. The superior dislocation is the usual one below the professional level of play and involves both the superior articular ligament of the acromioclavicular joint and the coracoclavicular ligaments. Its usual cause is a fall on the point of shoulder with forceful depression of the acromion. The arm is usually in moderate abduction, forward flexion, and internal rotation, i. e., the ball-carrying position. Such a dislocation is rarely the result of a blow directly on top of the shoulder because of the protection of the shoulder pads.

Cox[5] points out that in professional football a great number of anterior dislocations are seen, in contrast to college and high school football, in which practically none are to be found. There would seem to be two reasons for this: first, most professional players do not fall on the point of the shoulder because of previous training and developed agility; second, until recently, in professional football a player was permitted to get up and continue forward progress after his knee had touched the ground and, as he scrambled back to an erect position, an opponent or opponents would pile on his back, forcing his body forward and downward while the shoulder girdle was fixed by the extended arm or elbow.

Bateman[6] has pointed out that one result of superb mobility of the shoulder is frequent anterior dislocation and that the essential episode is the head of the humerus being forced against the weak anterior capsule. While the usual cause in civilian life is a fall on the outstretched hand in which the body weight carries forward and the elbow flexes, throwing the upper arm into abduction, external rotation, and extension, this only occasionally occurs in football because of training and the lack of a surprise situation. Here it is usually the result of a tackle in which the tackler looks away from his opponent and passes him too widely while attempting to grasp his thighs (fig. 2*C*); the momentum of the moving player and oncoming opponent then forces the abducted upper arm backward into full extension and levers it out of the joint. The inferior and the posterior dislocations have not occurred in my experience.

Sprain of the posterior capsule and posterior subluxation of the shoulder are frequent occurrences. They usually occur in unskilled players who have not learned falling techniques. The injury is most often sustained in ball carriers who fall on the point of the flexed elbow with the humerus in full forward flexion and moderate internal rotation. Force is transmitted upward through the humerus, and the humeral head is forced against the posterior capsule. Pain along the back of the shoulder joint and posterior instability of the shoulder may result. This injury does not often occur with falls on the outstretched hand, because there the elbow flexes and causes the shoulder to extend and the force is transmitted to the front rather than to the back portion of the shoulder capsule.

The internal rotator cuff may be damaged in several ways. In a fall with the arm near the side, force is transmitted directly upward, sandwiching the rotator cuff between the humeral head and the overlying acromion with resulting contusion. When the rapidly moving player is grasped by the arm and jerked, the downward or lateral traction against the fixed cuff muscles may strain or tear the muscular or tendinous fibers. In blocking, a strong blow on the abducted arm again may strain the fibers of the cuff.

Because of standard protective equipment, blows on the shoulder from above seldom traumatize the rotator cuff. Recognizable major tears in the cuff rarely occur in the football age group.

The upper arm is seldom affected by serious injury. Bruised muscles are frequent, and muscle strains are often encountered. Myositis ossificans occasionally develops in severely contused muscles. The radial nerve may be traumatized at the posterolateral aspect of the arm at the level of the middle third of the humerus.

Injuries to the elbow are usually easy to diagnose. Hyperextension sprain is common and results either from a fall on the outstretched arm or, more commonly, from a posterior blow on the fixed extended arm. Posterior dislocation has a similar mechanism. Other types of dislocation are unusual. Fractures of the medial epicondyle with tear of the medial ligaments are not infrequent; they follow a lateral blow on the extended elbow when the hand is fixed. In two cases seen this year, one player was grasping the jersey of an opponent and another had his hand on the ground and elbow extended while arising from the prone position. In contrast to nonsports injuries, lateral dislocation of the elbow is seldom found in conjunction with this injury. Radial head fractures result from the usual fall on the outstretched hand. The injuries associated with the throwing sports are scarcely ever encountered.

The forearm is seldom involved except through contusion. The hand is involved by the usual fractures, dislocations, and sprains with well-known mechanisms.

Pelvis and Lower Extremity

In general, the trauma sustained in the pelvis and lower extremity is more frequent and severe than that in the upper limb. In ligamentous injuries this results from the fact that the leg is fixed by the ground below and the body above when the force of a blow or indirect torsion strain is sustained. In contusions, the injury may be more severe than in the upper extremity because the part involved, the leg, is heavier than the arm, is probably moving with greater rapidity, and, of even greater significance, is superimposed by the entire body weight.

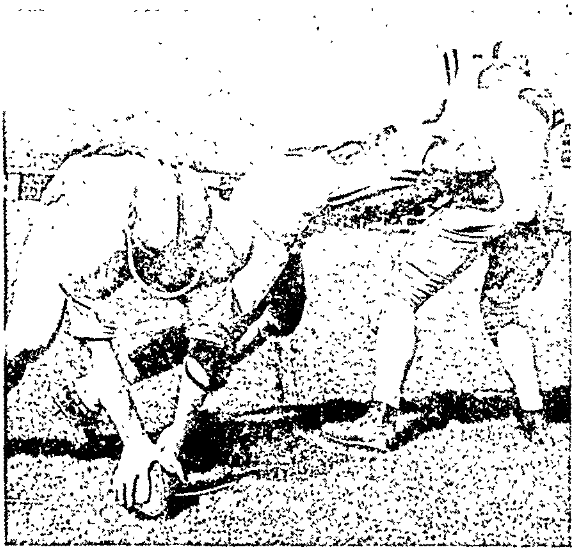

Fig. 3.—Mechanics of injury to iliac crest, flank, or lower chest wall. In this trap play, player 72 would have been faked out of position when ball was snapped and right guard would have pulled out behind center and would have struck defensive lineman from his blind side, forcing him out of play.

Contusions to the brim of the pelvis are called "hip pointers." These result from direct blows to the iliac crest and the musculature immediately above or below and are usually accompanied by hematoma formation (fig. 3). About 70% result from contact with other players (usually from "blind side" blows) or in pile-up situations.[1] In most instances they occur in spite of protective padding, but its absence or misuse will increase the likelihood of injury. The remaining 30% result from contact with other objects, such as the ground. With the exception of contusion of the greater trochanter of the femur, injuries to the hip region are few. The joint itself is seldom involved due to its protection by heavy muscles and the angle of application of traumatizing forces. Contusions of the thigh involving the quadriceps muscle are called "charleyhorses." These vary in severity from mild bruises to severe crushing injuries with rupture of muscle fibers and hematoma formation. When the latter occur in the vastus medialis, myositis ossificans may follow because of the intimate relation of this muscle with the underlying femur. In the majority of cases, the charleyhorse results from a strong shoulder block by the opponent, although the knee or foot may occasionally be the cause. It is more likely to occur if the thigh pads are loose or inadequate, but will often occur in spite of good protective equipment if the traumatizing force is great enough.

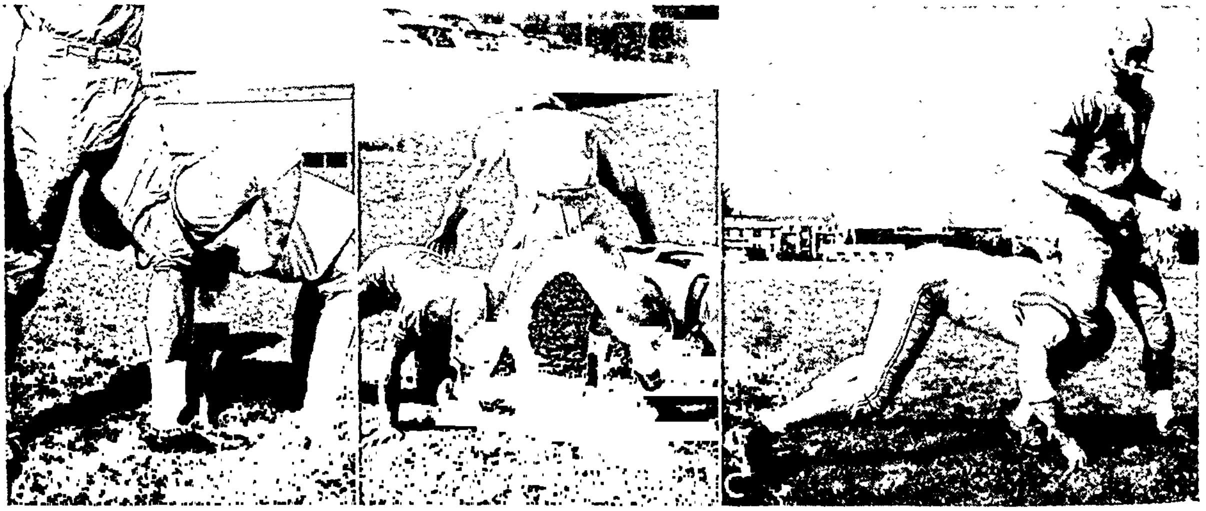

Fig. 4.—Knee injuries. *A*, contusion of knee by shoulder pad striking between thigh and knee pads. *B*, ligamentous injury to knee when defensive player 50 is subjected to "two on one" block by two offensive players. Normally, player would have his legs closer together and his feet in constant motion so that force could not be applied against his knees when his feet are solidly planted. *C*, player on left demonstrates typical clipping injury in which shoulder forces runner's knee inward and medial, while his cleats are fixed solidly to ground. Runner has complete loss of control and is subject to internal derangement of right knee. Injury varies, depending on whether force is applied from straight lateral or posterolateral position.

The knee presents a most vulnerable target for injury, due to its exposed position and to the fact that its movements are largely restricted to flexion and extension with little medial or lateral "give" (fig. 4). In contact injuries, 63% occur from the side, 28% from the front, and only 9% from the rear.[1]

Blows to the lateral side of the knee usually follow clipping, side-swiping, or trap blocking. To sustain ligamentous injury the foot must be fixed to the ground so that the force of the blow levers the inner side of the joint apart, with the outer bony rim acting as a fulcrum. If the foot is not fixed on the side of contact but the opposite foot is planted firmly on the ground, the force may be carried through to the opposite leg to lever the joint open laterally, rupturing the fibular collateral ligaments. The extent of cruciate ligament damage depends on the degree that the joint is opened on the side opposite the blow and the angle backward or forward of the lateral midline from which force is applied.

In frontal injury, contusions of the patella and suprapatellar region are incurred most frequently. The suprapatellar bursa which lies in the interval between the thigh and knee pads is most often injured by shoulder blows in tackling and blocking (fig. 4*A*). When a player takes blocks or tackles on his knees it is usually evidence of lack of ability, poor football preparation, or both. Bruises to the patella are often due to failure to use the protective knee pad; sometimes the pants are too tight, binding and restricting knee motion; often the pocket in which the pad should be inserted has shrunk from laundering until it is impossible to use the pad in it properly.

Contact at the back of the knee results in a straight forward or medial-and-forward force causing ruptures of the anterior cruciate and tibial collateral ligaments. In this instance, avulsion of the tibial collateral ligament at its distal attachment results in a tear which is greatest anteriorly; when it occurs at the femoral attachment it is greatest posteriorly; in the continuity of the ligament the tear may be at different levels in the superficial and deep layers of the ligament, and incomplete tears are located in the anterior or posterior side of the ligament in relation to their proximity to the upper or lower ligamentous attachment. In extremely severe contact injuries where torsion is present, the meniscus may be damaged. Muller,[7] reporting on 21 surgical cases of repair of severe ligamentous damage, states that in none of these was the meniscus injured. His findings suggest that twisting forces are not a major factor in most instances.

Noncontact injuries of the knee most frequently involve the meniscus and, to a lesser extent, the ligaments. They occur when the flexed knee is under a severe twisting strain, such as in the act of "cutting" where the player suddenly changes directions, often pivoting 90 degrees on the fixed foot. The question usually arises as to whether football cleats add to the likelihood of such an injury because of the fixation they afford. The weight of evidence points to the fact that aluminum, plastic, or composition cleats are readily withdrawn from the ground (in contrast to the old leather cleats) and are only dangerous when the foot is fixed, a situation which seldom occurs in the well-coached player. A second question which is often posed is whether ankle strapping, by restricting motion, causes more stress on the knee. Unquestionably it does but not to a degree which is dangerous to a properly trained player. Ankle injuries present no new problem as far as mechanism is concerned and will not be dealt with here except to point out the protective value of ankle wrap and ankle strapping; these reduce the incidence of sprain about 90%.

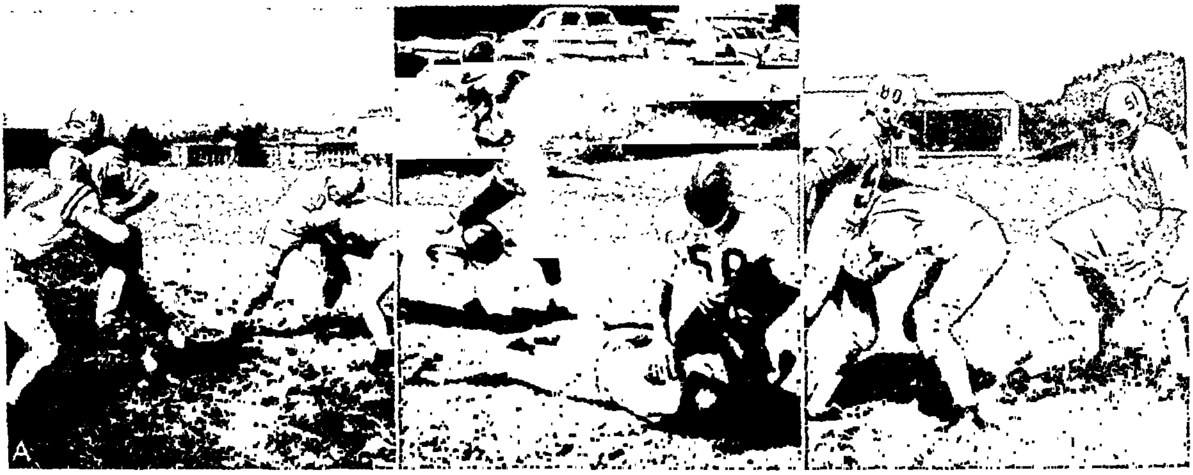

Fig. 5.—Injuries to head, neck, and spine. *A*, offensive player on left is out of football position while being tackled. Defensive player has used good technique, striking on-coming player immediately above belt line with his head, grasping his buttocks, and lifting upward to throw the ball carrier on his back. Helmet striking chin is likely to cause dental, facial, and neck injuries. Defensive player, driving in hard, will lift his head and shoulder, forcing his shoulder pads upward inside facial bar. This can result in facial injury or severe twisting of head and neck. *B*, player on left, tackling too low, is likely to sustain injury to trapezius muscle, cervical spine, or brachial plexus. Players on the right demonstrate second move of same play. Defensive player has completely lost control; spine is thrown into twist with possible back injury, and shoulder is rotated backward with possible contusion by offensive player's knee. He could sustain head or neck injury from offensive player's left knee. Situation is particularly bad in "gang" tackle. *C*, players on left demonstrate flexion injuries of the head, neck and back. Player 72 shows poor football technique by dropping his head on impact. This will result in blow on head plus acute flexion of neck. If player 80 moves forward he will raise his right thigh, throwing his opponent's back into acute flexion and exposing him to spinal injury through staggering force developed by oncoming knee. Defensive player on right is coming into his opponent too low—center of gravity is overbalanced, he has no lift to stop his opponent, and his head is twisted into position of possible neck injury. Spine is arched, which makes him liable to back injury as well.

The Head and Spine

Because of the frequency of facial injury and the seriousness of damage to the brain, the problem of trauma to the head has received more attention than that to any other body segment. Blows to the head may either injure the head itself or be transmitted to the spine, depending on their force and the angle of application (fig. 5). Blows are of two types: (1) the low-energy impact blow and (2) the high-energy impact blow. In the former, the current football helmet affords adequate protection against single or repeated blows, but these forces may be transmitted to the cervical spine where chronic sprain or cervical arthritis and its sequelae may result. The high-energy impact blow is the one which is potentially most dangerous and is responsible for the majority of fatalities. A study of location of the blow in fatal injury revealed[8] that "the left and right front side of the head incur 22.08 percent of all injuries. Blows on the top of the head (resulting in spine injuries) incur 18.83 percent. Internal injuries rank third with 18.18 percent. Traumatic blows to the back of the head incur 12.34 percent of all injuries."

The percentage of fatalities is relatively low (2 per 100,000 participants or 17.44 per year over the 1931-1956 period). Although no accurate statistics are available as to how these injuries have occurred, it is my feeling that the most lethal weapon in football is the oncoming knee. To give a rough example, a typical varsity fullback weighing 185 lb. (83.9 kg.) and running the 100-yard dash in 10.5 seconds was asked to kick a dynamometer with his knee. Standing, he could kick 500 lb., with one step 625 lb., and with two steps 725 lb. Add to this the increment of forces developed by rapidly moving players based on the formula "momentum equals mass times velocity" and a more realistic picture is presented. An aggressive, alert player may receive a serious head injury, and the weak, fatigued, or "loafing" player may be doubled up in flexion and receive serious spinal trauma.

Injuries to the spine are of two types: direct contusion and flexion or twisting injuries. The direct contusions are seldom serious, except for kidney blows. The indirect flexion injuries usually happen when a player (blocker or tackler) looks away from his opponent and is literally "doubled up" by the impact of the thigh or knee of an oncoming player. These may range from sprain to fracture of the cervical, thoracic, or lumbar spine. When a player loses body control at the time when strong body contact is faced, twisting injuries may be the result.

The face presents the single body area most vulnerable to injury. Here fractured teeth are most common, with the causative agent being the opponent's foot (25%), the head (18%), the knee (16%), and the arm (12%).[1] At a recent postgraduate conference, four outstanding college trainers seriously doubted the efficacy of present-day facial protection bars in reducing the incidence of facial injury; in fact, they felt that they might be responsible for a number of cervical sprains of the twisting type when grasped by an opponent, which frequently happens in spite of the 15-yard penalty rule.

Summary

Injuries due to football are the inherent risk of a vigorous body-contact sport. Early diagnosis is difficult under field conditions because of the pressure of time and lack of facilities for examination. Late diagnosis is handicapped by swelling and muscle spasm. A comprehensive understanding of injury mechanisms will often reveal the essential clues in the medical history that lead to prompt diagnosis and treatment.

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CONSEQUENCES OF LIGATING THE PULMONARY ARTERY.—In the absence of infection, the pulmonary artery does not become thrombosed beyond the ligature, but comes into communication with vastly enlarged bronchial arteries by means of precapillary peripheral anastomoses. . . . It is remarkable that the lung can survive ligature of both pulmonary arterial inflow and pulmonary venous drainage. Collaterals arrive from both sides, in a manner characteristic for each when it alone is stimulated to expand as described. It is astonishing that the ingrowth of newly formed vessels arriving transpleurally is orderly, in that arterial collaterals invariably establish connections with pulmonary arteries, and the venous collaterals invariably come to drain pulmonary veins. The forces that guide these vessels to their appropriate destinations are mysterious, but must be chemical, rather than purely mechanical. If they were simply mechanical, then the larger than capillary connections should be in the direction of the greatest pressure drop, *i. e.* from collateral systemic arteries to collateral systemic veins. Such "short circuits" have, however, never been observed in the vinylite casts. Instead, the course of the blood flow is apparently the most circuitous possible: from systemic collaterals directly, by precapillary anastomoses, to pulmonary arteries, to pulmonary capillaries, to pulmonary veins, and thence, by large anastomoses, to systemic collateral veins. More than one influence must, therefore, be considered in the attempt to reply to John Hunter's still perplexing question, asked 200 years ago, "What makes vessels grow?"—A. A. Liebow, M. R. Hales, and W. E. Bloomer, Relation of Bronchial to Pulmonary Vascular Tree, edited by W. Adams and I. Veith, *Pulmonary Circulation,* 1959.

TISSUE NECROSIS AND SLOUGH PRODUCED BY METARAMINOL BITARTRATE

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Tissue necrosis and slough occurred in a patient with generalized arteriosclerosis after intravenous infusion of metaraminol during which extravasation occurred along the course of the vein. Previously, multiple intramuscular injections of metaraminol had been well tolerated, as had intravenous infusions. It is suggested that, when metaraminol is used, all precautions against tissue damage, such as polyethylene catheters and phentolamine, should be used after extravasation in the presence of vascular insufficiency.

It has been reported that subcutaneous or intramuscular infiltration of metaraminol (Aramine) bitartrate causes no local tissue injury.[1] The purpose of this communication is to present a case of tissue necrosis caused by subcutaneous injection of metaraminol.

Report of a Case

A 65-year-old man was admitted to the Emory University Hospital, Atlanta, Ga., because of the sudden appearance of hemiplegia on the right side. He was said to have previously had transient episodes of slurring of speech and weakness of the right arm. No further medical history was available.

Physical examination revealed a blood pressure of 110/80 mm. Hg in the right arm, pulse rate 100 per minute; and temperature 98.6 F (37.5 C). There was a complete right-sided hemiplegia, with sensory loss on the same side and inability to speak or swallow. There was a loud systolic bruit heard over the left carotid artery at the angle of the jaw. A systolic thrill was palpable in the same area. A bruit of less intensity was heard in the same area on the right side. The heart and lungs were within normal limits. The abdomen was flaccid. The aorta could be palpated to the level of the umbilicus, but no pulsations were present below this level. No arterial pulses were noted in femoral or popliteal arteries or arteries of the feet. Pulsations were noted in the right radial artery but not in the left. Oscillometry revealed less than 0.2 of one unit of oscillation in the thighs, calves, and feet bilaterally at 60 mm. Hg. The lower right arm showed 2.5 units, upper right arm 2.5 units, lower left arm less than 0.5 units, and upper left arm 1.5 units at 60 mm. Hg. A diagnosis of generalized arteriosclerosis with left carotid artery thrombosis was made, and the patient was placed on therapy with anticoagulants.

On the ninth hospital day, a drop in the blood pressure was noted and 2.5 mg. of metaraminol was given intravenously. The pressure was then maintained with 10 mg. of metaraminol and 1,000 cc. of a 5% solution of dextrose and water for the next seven hours. After this, intramuscular injections of 2.5 mg. of metaraminol at two-to-four-hour intervals were continued for the next several days. On the 14th hospital day, the blood pressure again dropped to 70/40 mm. Hg and could not be restored by use of metaraminol intramuscularly. An intravenous infusion was then instituted in the right antecubital vein. Over the next three hours the patient received 1,600 cc. of the infusion containing 30 mg. of metaraminol per 1,000 cc. The infusion was stopped when subcutaneous infiltration occurred. To facilitate nursing care, the infusion was restarted in the right great saphenous vein at the ankle. A total of 75 mg. of metaraminol in 2,600 cc. of 5% solution of dextrose and water was given over the next 24 hours. The infusion was terminated when mild swelling of the lower portion of the leg was noted. Approximately nine hours later a discoloration was noted to extend along the course of the right great saphenous vein to the knee. In 72 hours the area had become dark and necrotic and drainage was noted. Treatment consisted of soaks, streptokinase-streptodornase (Varidase) topically, antibiotics parenterally, and débridement. Amputation was decided on, but the patient died of bronchial pneumonia before this could be carried out.

Postmortem examination showed generalized arteriosclerosis with occlusion of the terminal aorta just below the origin of the renal arteries, occlusion of the left internal carotid artery, and partial occlusion of the right internal carotid artery.

From the Emory University School of Medicine.

Comment

Tissue necrosis and slough occurred in the leg of a patient with severe atherosclerosis who was subjected to a slow intravenous infusion of metaraminol over a period of 72 hours. Concentrations of the agent used were not excessive, but there was subcutaneous extravasation along the course of the vein. Multiple intramuscular injections in the adequately vascularized upper arms and shoulders were well tolerated, as were intravenous infusions and one episode of subcutaneous infiltration. It seems logical, however, that any potent vasoconstrictor drug, when used in the presence of arterial insufficiency, is a potential cause of tissue necrosis.

It is suggested that, when metaraminol is used, all precautions against tissue damage, such as polyethylene catheters and phentolamine (Regitine)[2] in the local area after extravasation, should be utilized, particularly in the presence of vascular insufficiency.

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SOCIOCULTURAL STRESSES AND THE PHYSICIAN-PATIENT RELATIONSHIP

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The phrase "physician-patient relationship" is heard more today than ever before, and it seems destined to be the object of even greater interest in the immediate future. The concept is not new, but it has been undergoing considerable modification and clarification.

Throughout the greater part of the history of modern medicine the interaction between a physician and his patient has been known to be important. Few physicians today would challenge the observation that success and prestige in the community depend more on "the little things" that impress the patient than on mastery of the technical skills. "Old Doc Brown may not be up to date, but he understands me." "Dr. Jones has a way with people." How often have we all heard similar comments? And that old wheeze "bedside manner" still pops up from time to time. Have we not all at one time or another noted a seeming disparity between competence and popularity with patients? Perhaps we have even heard a somewhat embittered colleague mutter something to this effect, "I'm not trying to win a popularity contest, I just want to practice good medicine."

Having a "way with people" is certainly no substitute for sound medical principles. Nor, on the other hand, are these two in any way antagonistic. It is better to perceive them as complementary forces. One need not exert his imagination to recall valid reasons why a good physician-patient relationship is essential for optimal patient care. Only a few examples need be listed here.

"History is 60% of the diagnosis" has long been a medical axiom. But history-taking involves the always complicated process of communication, which, in turn, is heavily dependent on the relationship which exists between patient and physician. Communication, faith in the physician, and the content of the interpersonal relationship may well determine to what extent, or how accurately, the patient follows his physician's orders.

There is a growing awareness, especially among the behavioral scientists, that the total content of the physician-patient relationship might well influence the speed or extent of a patient's recovery from almost any form of illness. This hypothesis remains to be tested thoroughly, but research with burned patients, patients undergoing colostomies, and those with cardiac disease, to name a few examples, has brought significant findings to light. I anticipate that further research may well extend even to such areas as convalescence after appendectomy or cholecystectomy.

If one might accept as a given fact that a successful physician-patient relationship is, indeed, important in the over-all patient care, consideration can be given to the thesis of this paper: a number of social, cultural, and economic forces are acting to widen the gap between physician and patient. Furthermore, many of these factors which create

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stress in the physician-patient relationship are, paradoxically, elements which demand a narrowing of this gap.

Some of the elements which exert pressures predominantly on the patient side of this relationship will be reviewed first. Then, after considering those involving both sides simultaneously, the elements affecting the physician primarily will be discussed. The shift from one area to another will be almost imperceptible. This is as it should be. The interest here is in the meeting ground between patient and physician, and any stress (regardless of its primary focus) will be felt throughout the whole.

Publicity Pressures

A high proportion of newspapers now carry daily columns discussing health and illness. One after another, diseases, their symptoms and treatment, are sketched. Many leading magazines find it profitable to feature sections on medicine. Campaigns for funds and for the dissemination of information on poliomyelitis, tuberculosis, multiple sclerosis, muscular dystrophy, heart disease, cancer, cerebral palsy, arthritis, and influenza bombard the laity from all sides via every medium of advertising. (Diabetes even influenced the Davis Cup matches.) All of these lead to an increased awareness on the part of the laity of the potential hazards that jeopardize their chances for a long and healthy life. Anxiety is created, not only about their health but about their illness or their real or supposed symptoms. Mental illness statistics and the whole problem of mental health are claiming greater degrees of public attention, serving to bring the awareness of the possibility of developing a mental disease ever closer to each individual. Add to this the anxiety engendered by the succession of international crises, tension, and the threat of total annihilation of mankind, and the sum is the realization that our very existence is threatened—internally as well as externally.

All of these forces—increased medical knowledge, stimulated awareness of diseases, the threat of mental illness, and the imminence of annihilation—create an increasing need for the services of the physician. They also serve to make the patient more demanding (whether overtly or covertly) of increased time and attention from his doctor. Patients want more explanations, need more reassurance, and require more understanding.

These forces acting on the patient, although tending on the surface to draw the physician and patient closer together, actually make the existing gulf more apparent. A patient without these increased expectations, given a certain unit of the physician's time, will be more satisfied than the anxious and demanding patient given the same time. Perception of the physician-patient contact thus suffers a temporal distortion.

Further stress is exerted on the physician-patient relationship by the publicity so often given to attacks on the medical profession. Malpractice suits with skyrocketing claims and settlements make headlines. Sensational literature "exposing" hospital practices and physicians' conduct seems to be in vogue. Who can doubt the damage this does to the physician-patient relationship? Suspicion of the physician and diminution of faith in his skills are certain to take their toll.

Of course, there is another edge to this sword of damaging publicity. The physician finds himself more and more on the defensive—at times even apologetic. He is, at the same time, kept constantly aware of the threat of a malpractice suit. He is never certain just which of his patients may decide to take advantage of him; he may feel impelled to adopt an overly conservative style in all his therapy; and he is, in general, working under added pressures of anxiety. These factors may easily influence his relationship with all his patients. An optimal physician-patient interchange is undoubtedly based on mutual trust and respect. When suspicion, fear, tension, and loss of faith enter into one or both sides of the relationship, the entire relationship quite obviously suffers. Damage is done. The extent will depend on the degree to which these destructive elements are present.

Stresses due to Change in Therapy Environment

During the past 50 years, and especially during the span of the last generation, there has been a noted shift from home and family centered treatment to that of the hospital environment. Most of us will recall that during our own childhood the vast majority of illnesses were treated at home. The patient's family were constantly present to lend emotional support, to show their concern, and to be available at the patient's beck and call. The physician who attended the patient in the home became well acquainted with the family, the patient's living conditions, and other environmental factors. In essence, the physician was exposed to the psychological, social, and cultural factors, as well as the biological.

Today, as is well known, we are in the age of technological medicine. A far broader spectrum of diseases are treated in the hospital, where are concentrated a most imposing array of new techniques and technical personnel. Routines and procedures approach automation.

The technical advantages of hospitalization to the patient could not, for the most part, be duplicated in the home. Unfortunately, however, the psychological and social advantages of the family milieu are not sufficiently reproduced in the impersonalized hospital routine. The paradox is defined more sharply by our growing awareness that the dichotomy between the biophysical and the sociopsychological aspects of medicine is not a valid one. Man is at the same time a biological, a psychological, a sociological, and a cultural organism.

The stresses placed on the patient as the result of the change to a hospital environment are becoming more apparent as further sophistication in a more holistic approach to medicine is gained. It is realized, further, that in this age of technological medicine the physician is frequently denied the insights he previously gained from observing the patient in his home and with his family. It is evident, therefore, that the physician-patient relationship suffers stress bilaterally.

Problem of Specialization

Some of the side-effects of the current trend toward specialization are a further problem arising from our technological status. The mushrooming accumulation of medical knowledge precludes the attainment by any one physician of sufficient knowledge of all the specialties. Specialization is an obvious necessity; the only question concerns the optimal extent to which it should be carried. However, the very fact that there are general practitioners plus multiple specialties and specialists sets in motion considerable forces opposing a good physician-patient relationship.

The already doubting patient may harbor further suspicions that his family physician may not be quite qualified to handle his present illness. Or, if under the care of a specialist, he may wonder if the proper one has been engaged. Again a lessening of faith in the physician weakens the relationship. On the other side of the coin, it is conceivable that quite the opposite reaction may occur. A patient may enter his contract with a specialist with unjustifiably high expectations.

Effects of Prepaid Insurance

It is hoped that research may soon be initiated to determine the effects of prepaid insurance and group health plans on the physician-patient relationship. It is conceivable that under these circumstances there might be a tendency for people to view the physician as a salaried employee who is obliged to render all due medical care. Aside from the possibility of abuse of the medical plan and of the physician's time, there may well be other factors here that will have bearing on the relationship. For example, does the physician lose prestige to the extent that his leverage is decreased? Or, on the other hand, is there a tendency for the physician to perceive his patients as detached case numbers to be inserted in form 2A4XY? It may well be that more advantages than disadvantages will accrue from prepaid plans, but until adequate studies are done we must be cognizant of both possibilities.

Educational Lag

Returning to the matter of the accelerating accumulation of medical knowledge and the evolution of the holistic approach, it is noted that there are resultant educational lags. Practicing physicians are unable to avail themselves sufficiently of the growing mass of literature on the behavioral sciences. Medical schools, for that matter, are only beginning to include behavioral science material in the medical curriculum. Not the least of their problems derive from the dilemma of how to include this in an already overcrowded four-year program.

Partial solutions to many of the physician-patient relationship perplexities are becoming available as a result of significant interdisciplinary research in the field of social science in medicine. Adequate dissemination and implementation of this information has yet to be achieved. And the very absence of these new methods in their armamentarium causes many physicians to feel uneasy and insecure when confronted by psychosomatic cases. Lack of training in the behavioral sciences, and the resulting incertitude, may well reflect on relationships with patients.

Economic Stress

Stresses of economic etiology are equally apparent. Increased costs of living, of equipment, office rent, office personnel, malpractice insurance, etc., seem to leave the physician with but two alternatives, if he is to maintain his standard of living. He may (1) charge higher fees for services or (2) handle more patients. The first may arouse antipathy in certain patients, on the one hand, or compound the anxiety and reluctance that many physicians suffer from the discussion of fees, on the other. The second alternative increases the physician's pressures and fatigue and, at the same time, shortens the period of contact with each patient (many of whom need more, rather than less, time).

Sociopolitical Factors

I will not attempt to discuss the reasons, but physicians today seldom assume the community leadership roles of their predecessors. A family physician who was at the same time a leader in the community commanded prestige from his patients. He was respected for his active concern in the patient and in the patient's community. There was less chance of his having to labor under the stigma of a label of commercialism imposed by a suspicious or poorly informed public.

Conclusions

It has been the purpose of this paper to create further awareness of the sociocultural factors which cause stress in the physician-patient relationship. In revealing the widening gap between a patient and his physician it was not my intention to be pessimistic. There is too much of this already. Instructors of executive development courses say, "The definition of the problem is the biggest step toward its correction." Once we are aware that trouble does, in fact, exist, we must determine as precisely as possible the factors involved and how they may be remedied.

Examination of the problem of the widening gap in the physician-patient relationship demonstrates that forces are involved that necessitate assistance from beyond the ranks of the medical profession. Solution of this problem will be a task for research and other collaboration between social science and medicine.

THE PSYCHOTHERAPEUTIC APPROACH TO NEUROSIS IN THE PAVLOVIAN SCHOOL

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According to Pavlovian principles, the social factor is important in forming the personality. Hence, in a Marxist society there should be little conflict between society and the individual. Conflict can, however, result from disequilibrium between social forces and individual capacities. Deviations must be corrected by persuasion, suggestion, punishment, or in special cases by treatment. Three case histories illustrate the application of these principles in patients with anxiety reaction, depressive reaction, and hysterical conversion. Little attention is paid to infancy as a nucleus of later conflict, to sexual problems, which are solved by the relative sexual freedom of the adolescent, or to worries about the social security, which has to be accepted by the individual as it is offered by society. In this context, the psychiatrist and his patient, as products of the same society, have no choice, and psychotherapy simply aims to reconstruct the broken socially conditioned reflexes by verboverbal associations to a certain type of nervous system.

American writers whose studies refer to Pavlovian psychiatry and psychology appear surprised by the lack of information about Pavlovian psychotherapy in the Russian medical literature. Similarly, American textbooks of psychiatry or psychotherapy [1] do not mention any point of view about it. Salter presents a conditioned reflex therapy fragmentarily, but not quite in the Pavlovian conception. Laughlin [2] discusses Russian brainwashing without any special theoretical approach.

Inevitably then everybody has the impression that psychotherapy is not taken into consideration by the Pavlovians. Consequently, the question might arise as to the method of treatment and kind of psychotherapy they would use, if any. Generally the same drugs, shock treatment, and other physical therapies are used all over the world. Knowing that these cannot always heal the patients, this raises the question, "Are they treated in the best way?" Moreover, the fact that only the usual medication in the treatment of psychiatric disorders is referred to in the Soviet books [3] strengthens the impression that the patients are treated by no other means.

What is the explanation of the silence that covers Pavlovian psychotherapy? To understand the underlying facts of this situation is to understand the philosophical and practical approach to human relations in the Soviet type of society. It is necessary, therefore, to discuss briefly the formulation of the human concept in the dialectical materialistic view, which considers, according to Marx, "men as a product of circumstances and upbringing, and, consequently, changed men are products of other circumstances." [4] However, it would be a scientific error to interpret the above principle mechanically. The human being, in the materialistic philosophical concept, is not mere passive matter yielded to the power of environmental influences but an active purposive participant in it. Under these conditions the man creates his own milieu by his own work and activity, and any transformation in the content or form of everyday activity can produce changes in the psychic properties and in any stage of formation of mental processes.[5]

From City Hospital at Elmhurst.

Read before the periodic neuropsychiatric meeting, Beth Israel Hospital, New York, Dec. 4, 1958.

In this sequence of logical deduction, mental activity becomes the result of a report of interrelations between the human being and his environment. Generalizing the idea, human life became a new mode of existence of matter developed at a certain level. In supporting this point of view, it is best to quote directly from the materialistic philosophical interpretation of matter in motion according to Ananiev [6]; this will provide a clearer understanding of Pavlovian psychological orientation: There are different forms of movements of matter, from simple mechanical movements to the complex sensation. Sensation is an image of matter in motion as the most elementary element of consciousness directly reflecting the external world image. Space and time are regarded as the basic form of existence of matter in motion.[6A] This sustains the dialectical materialistic concept of quantitative changes being succeeded by qualitative changes as a transitory form of matter in motion to a new stage of existence. In other words, mental activity is conditioned by the form of existence of living beings and changes with the change in the existence, because "the matter is primary and the consciousness is secondary."[6A]

From this idea arises the well-known axiom of dialectical materialism that nothing can appear in consciousness which is not a reflection of some aspect of the objective world. But how?

We have to keep in mind that mental activity is the result of matter in its highest form of organization as a nervous system. The material basis for consciousness is the function of the brain. According to Pavlovians, consciousness is determined by existence but conditioned through the physiological activity of the nervous system. If mental activity is inseparably connected with the functioning of the brain, being a result of the latter, they might be studied by the same methods—materialistic methods. The successful representatives of this physiological school are Sechenov, Pavlov, and Ivanov-Smolensky. Russian psychiatry, oriented physiologically and sociologically, in its desire to find a solid ground in the explanation of the mental disorders had to consider the same approach.

Viewpoint of Russian Psychiatry

Although I have no intention of extensively discussing the point of view of Russian psychiatry, an outline of their general opinion is necessary for a better understanding of their psychotherapy. According to them, the general lines of mental activity of the brain are organized through unconditioned reflexes (which are inherited and, therefore, constant and phylogenetic) and through conditioned reflexes (which represent temporary bonds, highly variable in their connection, as the expression of the relations between environment and organism). The latter are acquired in the course of ontogenesis. Stated in broad terms, the conditioned reflex is formed due to an excitation which occurs simultaneously at two points in the central nervous system, making a connection or a coupling of them. Among the most important laws governing their formation, the laws of irradiation, concentration, and reciprocal induction play an important part in the explanation of the formation of the neuroses. According to these laws, mental disorders could be produced by disequilibrium between the processes of excitation and inhibition at the cortical and subcortical center, with the result of uncontrolled excitation foci which disorganize the normal brain functioning.

Pavlov [7] introduced the idea that the interplay of excitation and inhibition varies from individual to individual, depending on the type of nervous system. He categorized the mechanism of conditioned reflexes and their results according to the type of nervous system. As a sketchy review, there are four types: (1) strong unbalanced, (2) strong balanced, mobile, (3) strong balanced, immobile, and (4) weak. Every Russian psychiatry book discusses this at length.

The interrelation between the activity of the brain in the formation of cognitive processes and the type of nervous system might be summarized as follows: The sensation which represents the external stimuli is sent to the primary cortical sensory area, which has the function of analyzing, and it is synthesized by a secondary area into perception, into a conscious integrated nature, obtaining a stereotype of reaction.[8] The cognitive process, therefore, is always the reflection of the reality of the external world, but, as we know, there is a potential conflict between the amount and the quality of excitation and inhibition, as a physiological process in the mechanism of cerebral activity, in a certain type of nervous system. It remains necessary for the psychiatrist to recognize the quantity and the quality of stimuli that can be sustained by the individual with his particular type of nervous system in the formation of the dynamic stereotype. In support of the above idea, one has to recall the experimental work of Ivanov-Smolensky, who produced in the laboratory so-called neuroses of excitation and inhibition in healthy human beings.

In corroborating their view about the type of nervous system, Saprykin and Milerian [9] found that a conditioned reflex, established by pressing a colored button and the resulting appearance of a light of the same color, easily became strict; and by changing the speed of reaction they introduced the element of differentiation of conditioned stimuli in determining the type of nervous system. (The basic work was done by Ivanov-Smolensky.)

To summarize the general facts presented above, the psychotherapist has to keep in mind both the dialectical materialistic orientation of the society in which the individual is a purposive actor and the reaction of the individual, with his distinct personality, including his type of nervous system.

The physiological interrelation between the external world and the nervous system is presented by Bâkov,[10] referring to Pavlov, in this way: "Any element in the external environment which is indifferent for the organism may, under a certain condition, become a factor acting upon its central nervous system through the receptors. Under this condition, the action of neutral elements of the external environment may produce change in the organism." In line with this, Ilyina[11] made the same strong connection between the social reaction and the different types of nervous system (experiments correlating galvanic skin reflexes and the establishment of social contact).

Social Factor in Development of Personality

Briefly, all the Russian psychological papers, emphasizing dialectical materialistic thinking and physiological Pavlovian orientation, stress the importance of the social factor in the formation of personality. If this is so, first, in the Russian-Marxist society what may influence the development of the individual? Second, since the Russian psychiatrist is convinced that the personality is developed through social interaction, according to the type of nervous system, how will he analyze the social factor as a possible source of conflict for the individual?

The point of departure is the materialistic theme that the consciousness is a reflection of the objective world, is formed by the process of labor, and appears during human activity. This means that the society influences the individual by its people and by its principles.[12] But what are the principles of this society? Can these principles of society become a source of conflict between the society and the individual?

To understand all these remarks and the position of the psychotherapist, we have to take a brief look at the Russian-Marxist social organization. A society with an economic and social organization planned and directed by the central government implies in its structure, as a decisive factor, that the state has a dominant role over the individual. In this situation, the individual, regardless of his aims, is subordinated to the interest of the state. This society has strict regulations and dogmas in which the individual is supposed to believe, without hesitation, after a long process of learning and education organized by the state. The child's upbringing, education by the school, literature, radio and television, and social life are directed to form these temporary nervous bonds (conditioned reflexes) in supporting the aims of the state and stimulating the individual to them. Even the instinctual drive is channeled according to the necessity of the state.

Any deviation, sometimes unintentional, has to be corrected by persuasion, suggestion, or any form of social punishment. The individual, as in any society under social pressure, may present signs of neurotic reaction and, fighting more or less consciously and deliberately against the unlimited state authority, escape into sickness. The psychiatrist, using scientific methods, has to establish a balance of forces between the individual and the state, thus recuperating the individual for society. But the psychiatrist himself, as a member of this society, cannot admit that the conflict is caused completely by the social organization. According to philosophical materialism this society has solved the conflict of interests of the individual and society. Only the social productive relation and economic factors in the capitalistic order can be a source of personality conflict (Marx). The psychiatrist does not overlook the social factor, but, since it is a generalized phenomenon to which all the people have to adjust successfully, he admits that only some of them might have problems because of their type of nervous system, where the external stimuli might form disturbed conditioned reflexes by prolonged inhibitory reaction or by overexcitation. If the state is to carry out, successfully, social and philosophical education for almost all the people, it remains for the psychiatrist to continue the work of the state by shaping personalities.

In what way will psychotherapy help him? It is generally accepted that the purpose of psychotherapy is to influence by means of words the state of mind of the patient, thus making him accept society and integrate himself better into it. The difference between the Freudian and Pavlovian psychotherapeutic approaches is the difference in interpretation of conflict. According to Teplov,[13] behaviorist psychology is mechanistic because it interprets all psychological phenomena in physiological terms. Nevertheless, Watson asserts that there are subjective processes of human consciousness which cannot be studied by objective methods. Zalkind,[14] in trying to describe Freudian psychology, defines it as oriented toward the past. He goes on to say: "The past is at war with the present and is more powerful than the present. The conscious is subordinated to the unconscious. Man is preserved from the demands of society in a private little world in which he constitutes a special strategy of behavior. If the man is a pawn of internal elemental forces, what sort of result will we get?" Furthermore, he asks himself, how can we use the Freudian conception of man for socialist construction? The psychiatrist cannot allow the patient to sustain the idea of guilt by the unprofitable internal conflict of his own insight. The psychiatrist has "to quickly take people, socially open and easily collectivised, and completely transform their behavior," according to the general social directive. Psychotherapy will help him to reestablish the broken social conditioned reflexes by establishing a new verboverbal association, according to his type of nervous system.

Case 1.—A young male worker, 30 years of age, in good health, with a healthy background, was politically attached to the aims of the worker class.

He was without training except for seven years of elementary school and was promoted by the government after two years of political law school to a high social position as a judge. The tremendous responsibilities, with the difficult burdens of his occupation, had completely changed the life of the patient. He worked between 16 and 18 hours a day to keep up his social duties. After dealing with difficult justice problems, having to contend with the skill of lawyers, the pressure of the party, and the making of decisions, the patient started to present signs of anxiety, irritability, sweating, and precordial pressure. Over a period of two years, according to his complaints, he was seen at many medical services and was always considered as a cardiac neurotic.

At the time under discussion, while dealing with a difficult political, economic trial involving the lives of some innocent people, he started to doubt his abilities to give a right decision. He started the investigation two weeks previous to this trial, but he could not participate in any decision. The anxiety increased, he could not sleep well at night, and he began to experience feelings of foreboding that something terrible would have to happen to him. On the night prior to the trial, the patient, while reading papers presenting an accusation against some party members trapped by inexperience, identified with them and compared their situation with his, whereby he might be trapped by the lawyer. The patient became excited, with obsessional thought and hypnagogic hallucination. The patient was given a diagnosis of anxiety reaction, with a strong-unbalanced nervous system. The treatment was psychotherapy and sleep therapy to induce protective inhibition.

On looking into the patient's history, one finds that the change of his life from a manual to an intellectual worker increased the imbalance of the mechanism of cortical activity by excessively increasing the process of differentiation. Accordingly, he was advised to change his job to a less intellectual and theoretical one. The preferred procedure, in this case, was to soothe the conflict between him and the authority of the society represented by the party and to strengthen the socially conditioned constellation of motivation through other useful work with less excitatory differentiation processes.

To better understand the psychotherapeutic mechanism, it is necessary to again refer to the Pavlovian theory of motivation action. Human action is considered to be determined by any kind of status motive and directed toward a special goal. According to this conception all motives are derived from these needs, whether they are moral or material. The society holds all the aims in each structure, as well as the choice of those to whom permission to fulfill them might be given. The process of attaining the goal (being chosen) is directed by the social education with its special rules, established by the authority. In this condition, the action is determined by the conscious belief accepted by the society. It is a belief in the social structure of the state and the ability to arrive at a decision in accordance with the personal possibility. The role of the psychiatrist is to weigh the potentiality of the nervous system to support the social burden of the goal.

Case 2.—A woman, 28 years of age, was admitted to the hospital for a depressive reaction. The history indicated a normal childhood and adolescence. She successfully attended all the required schools and obtained a title as engineer. In college, she fell in love with an officer in the army. They were married, but at the end of the studies she was sent to a plant hundreds of miles from her home. As a matter of fact, not only was her marital life broken but even the love became doubtful. Under the new condition, she started to feel isolated and alone, at times presenting a spell of sadness. Her work, in her opinion, was not efficient and she was warned many times that she was a delayer of production. The place and the people were completely unfriendly to her and, even more, she missed the comfort of her home city. She could not give up the job because she might be sued by the state as a saboteur. Gradually, she lost any interest in life and wanted to commit suicide. When brought into the hospital, she was given a diagnosis of depressive reaction, with a weak type of nervous system.

The psychiatrist, by psychotherapy, worked to strengthen her social motivation above her personal and emotional needs by explaining that the conflict was caused by her weak nervous system and that the party could not trust this in any emergency. The social pressure was too strong to permit any deviation from the official line. Any fight to change position, city, or place of work is useless without official permission. She was taught to adjust herself to the need of the collectivity, to adapt to the new condition by solving the personal problem in accordance with the official requirements. The patient was cured.

Infancy and Childhood as Source of Neurosis

It is surprising to observe the lack of attention paid by the Pavlovians to infancy and childhood as a nucleus of later conflict and problems of adult neurosis. The psychological approach is limited to follow strictly the general pattern of education imposed by the state. The well-known conflict between the child and its parents has to be shifted to an abstraction—the collective authority. The long series of authority figures starts with different nurses in nursery homes and is continued with the teacher in kindergarten, elementary school, professional training, and so on, obtaining an impersonalized authority figure which helps the formation of the notion of symbolic authority. However, Pavlovians agree that the development of the personality is influenced by the social relationship in family life, education, and working collective.[12] According to them, childhood is a period in the life of the organism when, on the basis of the connection formed between organism and environment during phylogenesis, there is intensive building up of a structure of temporary connection that is acquired in the course of individual life.[15]

The individual at birth is under the influence of the environment in what he reacts to, with his anatomic-physiological nature and his innate interests. From the early motor and sensory activity of infancy, after the formation of the self-image, the child shifts gradually by developing his interests to the general and social meaning of the activity. Development is achieved by a process of imitation, as an expression of the unconditioned reflexes, and verboverbal nervous connection, as referred to the second system of signals.[16]

The early collective life, with its rigid taboos and obligations, completely changed and modeled the behavior and shaped the personality, according to the social concept. Therefore, the claims of the Russian psychiatrist and psychologist Rudik [17] about the typical new Soviet man who puts all his life in the service of the society, excluding his personal status motives, are not surprising. Even if their personal motivation is not excluded, they have to put in time in the interest of the state. Generally, this is the meaning of their Stakhanovism. Zachepitsky [18] agrees with the theory that neuroses are conditioned by psychic trauma, but the trauma is referred to early human social relations which might be in the early childhood.

The conflict could not be found in the childhood trauma of sexuality; the problem of the Oedipus complex is denied by the Russian psychiatrist as influencing the development of the individual, since the interest of the child, in that period, is directed toward the socialization of his needs. The solution of the sexual problem cannot represent a nucleus of the conflict, since relative sexual freedom helps the teen-ager to solve the problem. His interests and preoccupations are to cope with other dominant social needs and aims. The problem cannot represent a conflict for the patient if the society gives immediate, efficient, and harmless solutions. Therefore, all the efforts of the psychiatrist are directed to the dominant problem of the neurotic patient: to solve the social conflict of security.

Because the security of childhood is continued by social security, accorded by the state, the nucleus of the conflict is between the individual and the state and not in the individual-parent relationship. The state is entitled to affection, which is expressed by the individual through the quality and quantity of work done, and the state, consequently, gives security to the individual. The psychiatrist has to rework the process of socialization of personality in the light of the patient's nervous system. In reestablishing the socially conditioned reflexes, the psychotherapist uses the resources of mental activity of the patient but not of his unconscious. The Russian psychiatrist does not accept the idea of the unconscious as it is understood in the West.

This hypothesis is not accepted, but this does not mean, as many believe, that the Pavlovians do not accept the concept of forgotten repressed memory. They agree with the psychological materialistic theory of the amnestic mechanism of the forgotten memory. The memory represents all the past experiences obtained through perception. The perception reflects the object by the mechanism of the sensation, analyzed in the sensory cortical area and synthesized into the secondary or perceptal area. The memory represents its storage. It is influenced by the attention, which is based on induction of the psychological process of excitation and inhibition. The mneme has an affective color, which either will or will not help the process of recollection. Participation of the mneme in formation of the personality is through the process of learning and education, in other words, by experience. Therefore, it cannot constitute an element of unconscious conflict, since an unpleasant experience is not forgettable as an element of conflict, while a pleasant one might not be forgettable because of the importance of the experience to the patient. Repressed memories do enter in the formation of the stereotype reaction but cannot enter in the mechanism of the neurosis formation as a source of conflict, as long as they are forgotten experiences. At the moment of their reappearance as a part of the conflict, they are conscious. The process of neurosis formation remains an imbalance between overexcitation and the weak inhibitory process. The imbalance contributes to unbalanced stereotype reaction formed as a disequilibrium between their own demands and their resources. In this light, the duty of the psychiatrist is to look through the life history of the patient to study the imbalance between motivation and resource reality as a possible cause of the conflict. Accordingly, for example, hysteria is regarded as a condition which might appear in children for whom the environment has acted as a factor of too much excitation on the nervous system, regardless of whether their response is negative or positive.

Case 3.—The patient, a 27-year-old man with a bachelor's degree who had obtained a position as an employee in a plant, came to the hospital for paralysis of the right arm which appeared in the morning while going to work. The social history showed a cranky child who always did things in his own way and was very upset when he could not get what he wanted. In school he was an average student, obtaining many good marks fraudulently. He remembered an incident at the age of 15 when he fainted when he could not do a difficult task. Then he received attention and care which gave him a pleasant feeling. As a matter of fact, he repeated the same pattern of reaction whenever he could not solve his problems. (For instance, he fainted many times after he could not pass the examination to enter a university and was obliged to face life by working as an employee.) The conflict increased because his family always wanted him to have a brilliant career. The solution of the conflict was always found in his daydreaming. Going into the army, he had a hard time and spent a long time in the hospital for various sicknesses, more or less real. After the termination of his military service, he held various jobs until the last one. The unpleasant condition of the job appeared clear from his presentation. According to the law, he could not resign, and his hate against the job increased day by day. On the morning previous to the paralysis accident he had a conflict with his superior. He could not obtain a leave. The next morning he presented a paralysis of the arm, developed during the night.

The psychiatrist directed his work to reconstructing the personality according to the patient's real responsibilities in the social organization. His life was analyzed, point by point, showing him his inadequacy to cope with the situation of being promoted to a better position. The paralysis was treated as a syndrome with a short course, and healing was suggested as obligatory. Social motivation was emphasized in supporting the resolution of the conflict.

Comment

In conclusion, the psychotherapeutic work of the psychiatrist is to strengthen the social pattern established by the society and to look on the patient as an integral whole with a functional relation to the external factor activity. For the psychiatrist, the environment requires a particular dynamic character because the individual is in society which puts its seal on his development.

The psychiatrist and the patient, as products of the same society, have no other choice. The psychiatrist has to have a determined position in relation to pseudo-scientific manifestations of other ideologies. Even neutrality in the war against the other theory (Freud) is as contemptible and impossible as a tendency to compromise with it. A new orientation based on a nonmaterialistic philosophical doctrine means a mistake in science, and such a mistake is a political error.

This doctrine has to be satisfactory to the Pavlovians because it gives them the explanation of the creative processes which, according to Boico, are explained on the hypothesis of interaction of conditioned reflexes, a process that occurs partially as a result of spatial coincidences of excitation in the cerebral cortex cell. Different systems of connection function simultaneously and redistribute the nervous impulses entering the brain by forming, at a new qualitative level, the mental process.[16]

Summary

According to the Pavlovians, mental activity is a result of the function of the brain and is determined by the person's existence. Since it is mediated by the physiological mechanism, it has to be studied with the same materialistic methods, conceptualized by Pavlov. Since it is determined by the existence, it is influenced by the external world—society.

The psychotherapeutic approach has to be physiological and materialistic, philosophical and dialectical. It has to reestablish and reconstruct the broken socially conditioned reflexes by verboverbal associations to a certain type of nervous system. Any other approach, based on any nonmaterialistic philosophical, dialectical, and non-Pavlovian concept, is a scientific error.

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DIHYDROSTREPTOMYCIN DEAFNESS

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Cases of irreversible hearing loss attributable to dihydrostreptomycin are continuing to occur, usually without the knowledge of the prescribing physician, because of the latent period of from several weeks to as long as six months between administration of the drug and onset of the hearing loss. There is no known effective treatment for this type of nerve deafness. In view of the ototoxicity of dihydrostreptomycin and, in particular, in view of the unique latent period, this antibiotic should be omitted from commercial combinations of antibiotics or, if it is included, its presence should be clearly indicated in the name.

Four years ago attention was called[1] to the permanent deafness that may occur after administration of comparatively small doses of dihydrostreptomycin. Unfortunately, cases of irreversible hearing loss attributable to this antibiotic are continuing to occur, usually without the knowledge of the prescribing physician, because of the latent period of from several weeks to as long as six months between the administration of the drug and the onset of the hearing loss. This latent period is unique for dihydrostreptomycin. Other known ototoxic drugs, including quinine, streptomycin, neomycin sulfate, and kanamycin, produce an impairment of inner ear function usually immediately during or shortly after the time of administration.

The ototoxicity and the unique latent period before the onset of ear symptoms were first pointed out for dihydrostreptomycin in 1951 by Glorig,[2] who found that approximately one-third of a group of tuberculosis patients who received dihydrostreptomycin in doses of 2 to 7 Gm. weekly over a period of several weeks subsequently developed a hearing loss that began in some cases as late as five months after the medicament had been given.

Because of the known toxic effects of streptomycin on the vestibular function and the toxic effects of dihydrostreptomycin on the cochlear function, it was thought that by combining streptomycin and dihydrostreptomycin in equal parts the total dosage of each would be reduced and the undesirable vestibular and auditory toxic reactions would be eliminated.[3] What was first thought to be a logical therapeutic improvement has actually turned out to be an added danger, particularly when drug companies market multiple combinations of antibiotics combining penicillin, dihydrostreptomycin, and streptomycin under names that do not clearly indicate the presence of dihydrostreptomycin. In some cases injections of such combinations have been given not for severe infections as lifesaving measures but prophylactically in uninfected surgical patients or for mild common infections, and their administration has resulted in irreversible nerve deafness.

We have observed 32 cases of permanent hearing loss after the use of dihydrostreptomycin since the first report four years ago (see table). Additional cases of permanent hearing impairment, probably the results of administration of this drug but in which the total dosage or the exact preparation used was not known, have been encountered but are not included in this report. Cases 1-6 are from the office of Drs. H. House, W. House, and Hildyard; case 7 is from Dr. Schuknecht; cases 8-10 are from Dr. Shea; and the remaining cases were observed in the office practice of Drs. Shambaugh, Derlacki, and Harrison.

Summary of Thirty-two Cases of Dihydrostreptomycin Deafness

Case No.	Age, Yr.	Commercial Preparation Administered	Reason	Total Dose, Gm.	Time Before Onset of Hearing Loss After Drug Was Given, Mo.	Average Loss for Speech Frequencies, Db.
1	54	Dihydrostreptomycin	Cystitis	5	2 days	52, bilaterally
2	31	Dihydrostreptomycin	Influenza	3	2	40, bilaterally
3	65	Dihydrostreptomycin	Tuberculosis	60	During treatment	23, bilaterally
4	66	Dihydrostreptomycin	Tuberculosis	60	3	33, bilaterally
5	22	Combiotic	Influenza	1.5	3	35, bilaterally
6	65	Penicillin, Dihydrostreptomycin	Influenza	8	1½	80, right ear; 63, left ear
7	35	Dicrysticin	Tuberculosis	18	3	50, bilaterally
8	20	Combiotic	Cold	1	Immediately	35, bilaterally
9	40	Dihydrostreptomycin	Pleural effusion (smear positive for acid-fast bacteria)	15	2 (after last injection)	15, bilaterally
10	29	Dicrysticin	Bronchial asthma	2	Several	28, bilaterally
11	54	Neomycin, streptomycin-dihydrostreptomycin	Nephritis	6 4	3	30, bilaterally
12	51	Districillin	Panhysterectomy	18 cc.	4	25, bilaterally
13	41	Dihydrostreptomycin	Furuncles	2	1	42, bilaterally
14	70	Combiotic	Upper respiratory infection	3	5	50, bilaterally
15	64	Streptomycin-dihydrostreptomycin	Eye infection	7.5	4½	30, bilaterally
16	21	Dicrysticin	After appendectomy	2.5	5	30, bilaterally
17	29	Streptomycin-dihydrostreptomycin	Urinary infection	20	1	40, bilaterally
18	45	Combiotic	After hysterectomy	4	¾	57, bilaterally
19	39	Strocillin	After hysterectomy	8	3	37, bilaterally
20	54	Durycin	Pneumonia	6	4	50, right ear; 55, left ear
21	5	Streptomycin-dihydrostreptomycin	Meningitis, pulmonary tuberculosis	150 for 11 mo., 1 daily after	Indefinite	Total deafness
22	38	Combiotic	After appendectomy	3	2	48, right ear; 60, left ear
23	66	Strocillin	Urinary infection	17	5	30, bilaterally
24	45	Dihydrostreptomycin	Pneumonia, pneumonectomy	30	Time of therapy	85, bilaterally
25	16	Dihydrostreptomycin	Mononucleosis	30	4	20, bilaterally
26	31	Dihydrostreptomycin	Tuberculosis	100	6	88, right ear; 95, left ear
27	53	Dihydrostreptomycin	Sinusitis		Few days	60, right ear; 65, left ear
28	57	Dicrysticin	Bladder infection	14.5	3	50, bilaterally
29	46	Dihydrostreptomycin	Hernia, pneumonia	2	1	40, bilaterally
30	33	Streptomycin-dihydrostreptomycin	After appendectomy	21	¾	55, bilaterally
31	21		Encephalitis	14	4	30, bilaterally
32	29	Dihydrostreptomycin	Dry socket	7 injections	½	32, bilaterally

Report of Representative Cases

Case 18.—A woman, aged 45, with apparently normal hearing, was given eight doses of Combiotic (penicillin and dihydrostreptomycin) over four days as prophylactic therapy after an uneventful hysterectomy. The total dosage of dihydrostreptomycin was 4 Gm. Three weeks after the last injection of the antibiotics hearing loss was noted. The patient's hearing declined rapidly within the course of several days and then stabilized at the level shown in figure 1.

Case 19.—A woman, aged 39, had apparently normal hearing and received 16 doses of Strocillin (penicillin and dihydrostreptomycin) over an eight-day period after a hysterectomy. The total dosage of dihydrostreptomycin was 8 Gm. Tinnitus began 12 weeks afterward, and hearing loss was noted four months after the last dose. This patient was a telephone operator and became considerably disabled and depressed over her loss in hearing (fig. 1).

Case 28.—A man, 57 years of age, had cystitis and apparently normal hearing when he received over a two-week period Dicrysticin (procaine penicillin G, buffered crystalline sodium penicillin G, streptomycin, and dihydrostreptomycin) containing a total of 14 Gm. of dihydrostreptomycin. Hearing loss was noted within three months and became stable at the level shown in fig. 2.

Case 12.—A man, aged 41, suffering from furunculosis, had apparently normal hearing. He received four injections of dihydrostreptomycin, totaling 2 Gm., and noted hearing loss four weeks later (fig. 2).

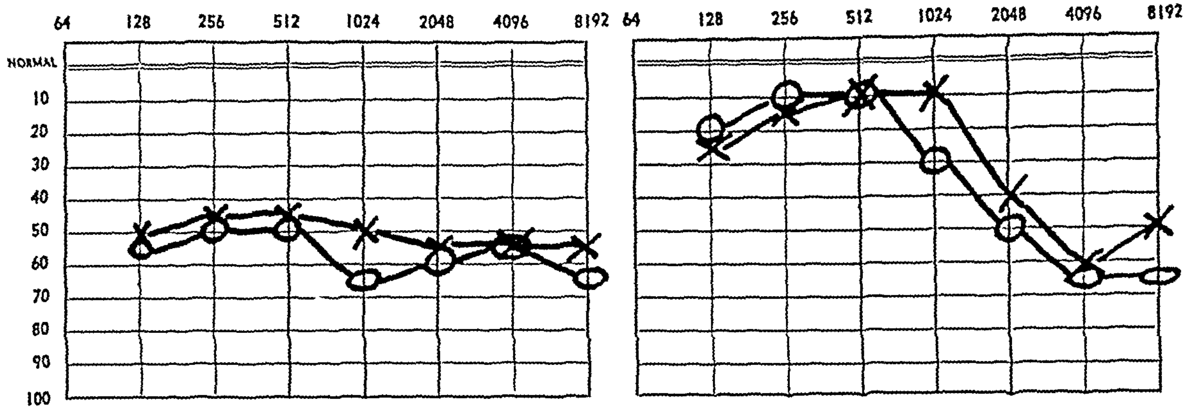

Fig. 1.—Results of hearing tests by air-conduction audiograms in cases 18 and 19. *Left*, case 18, audiogram showing loss for speech frequencies 512, 1,024, and 2,048 between 45 and 65 db. in both ears (*right ear, circles; left ear, crosses*), onset three weeks after receiving 4 Gm. of dihydrostreptomycin over four days. Discrimination score in right ear was 8% and in left ear, 18%. *Right*, case 19, audiogram showing loss for high frequencies greatest at 4,096 with discrimination score in right ear of 48% and in left ear of 72%, onset four months after receiving 8 Gm. of dihydrostreptomycin over eight days. (For good use of hearing aid discrimination score should be 90 to 100%. Score of less than 50% indicates great difficulty in understanding speech with or without hearing aid; score as low as 18% indicates that it is almost impossible for patient to understand speech by any means.)

Comment

Due to the latent period that frequently occurs between the administration of this antibiotic and the onset of the irreversible hearing impairment, dihydrostreptomycin is a particularly treacherous ototoxic drug. The small total doses of dihydrostreptomycin, 2 or 3 Gm., which effected permanent irreversible hearing loss in some of the patients observed (see cases 2, 5, 14, 22, and 29 in table), are noteworthy. In some cases the injections of the antibiotic, usually in combination with penicillin and streptomycin, were given not as lifesaving measures, but prophylactically in uninfected surgical patients or for mild, self-limiting infections such as influenza. The prescribing physician usually had not the remotest idea of the eventual disastrous results.

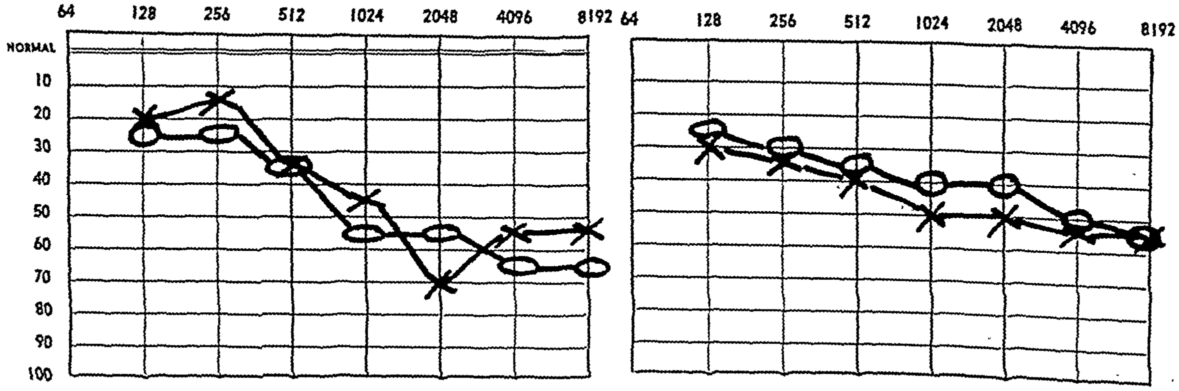

Fig. 2.—Results of air-conduction audiograms in cases 28 and 13. *Left*, case 28, showing loss of 35 to 70 db. for speech frequencies of 512, 1,024 and 2,048 in both ears, onset three months after administration of 14 Gm. of dihydrostreptomycin over 14 days. Discrimination score in right ear was 78% and in left ear, 40%. *Right*, case 13, audiogram showing loss of 35 to 50 db. in both ears, onset four weeks after administration of 2 Gm. of dihydrostreptomycin over four days. Discrimination score in right ear 74%, left ear 76%.

The typical hearing loss was one of high-frequency impairment, involving the lower frequencies to a lesser degree and varying with the dosage and the individual susceptibility. In many cases a mild or moderate hearing loss in the pure tone audiogram was accompanied by a disproportionate impairment of speech discrimination, so that the patient's ability to understand speech was more impaired than the pure tone loss would indicate and seriously affected or even prevented effective use of a hearing aid (fig. 1).

Such commercial preparations as Bicillimycin, Cillimycin, Combiotic, Crysdimycin, Dicrysticin, Dihydrocillin, Distrycillin, Durycin, SRD, and Strocillin* are mixtures containing dihydrostreptomycin, usually in combination with penicillin and streptomycin. All of these have been followed by permanent hearing loss in cases that we have observed.

There is no known effective treatment for this type of irreversible nerve deafness. The most that can be done for these patients is to make extensive trials with amplification of sound through hearing aids and instruction in lip reading to fill in the gaps missed by audition.

Because of its known ototoxicity, neomycin is now recommended for nonparenteral use except as a lifesaving measure. Kanamycin may soon be similarly restricted. In view of the less well-known ototoxicity of dihydrostreptomycin and, in particular, in view of the unique latent period before the onset of deafness, this antibiotic should be omitted from commercial combinations of antibiotics, or if included its presence should be clearly indicated in the name.

Since streptomycin is as effective as dihydrostreptomycin for gram-negative and acid-fast infections,[4] and since toxic reactions from streptomycin occur immediately and are more easily recognized and less permanently disabling, there seems to be little reason to use the more dangerous drug.

55 E. Washington St. (2) (Dr. Shambaugh).

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*Bicillimycin: 600,000 units of procaine penicillin G, 300,000 of potassium penicillin G, 0.25 Gm. of streptomycin, and 0.25 Gm. of dihydrostreptomycin; Cillimycin: 300,000 units of penicillin G, 100,000 of crystalline penicillin G, 0.25 Gm. of streptomycin, and 0.25 Gm. of dihydrostreptomycin; Combiotic: 400,000 units of penicillin and 0.5 to 1.0 Gm. of dihydrostreptomycin; Crysdimycin: 600,000 units of procaine penicillin G, 0.5 Gm. of streptomycin, and 0.5 Gm. of dihydrostreptomycin; Dicrysticin: 300,000 units of procaine penicillin G, 100,000 of buffered crystalline sodium penicillin G, 0.25 Gm. of streptomycin, and 0.25 Gm. of dihydrostreptomycin; Dicrysticin Fortis: 300,000 units of procaine penicillin G, 100,000 of buffered crystalline sodium penicillin G, 0.5 Gm. of streptomycin, and 0.5 Gm. of dihydrostreptomycin; Dihydrocillin: 300,000 units of procaine penicillin G, 100,000 of crystalline penicillin G, and 1 Gm. of dihydrostreptomycin; Distrycillin: 400,000 units of procaine penicillin G, 0.25 Gm. of streptomycin, and 0.25 Gm. of dihydrostreptomycin; Durycin: 400,000 units of procaine penicillin G and 0.5 Gm. of dihydrostreptomycin; SRD: 400,000 units of penicillin G and 0.25 Gm. or 0.5 Gm. of streptomycin and dihydrostreptomycin; Strocillin: 400,000 units of penicillin and 0.5 Gm. of dihydrostreptomycin.

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FEEDING THE POTENTIALLY ALLERGIC CHILD.—A potentially allergic child is defined as one having one or more allergic parents or siblings. . . . Recent surveys show that in some instances as much as 25% of the pediatrician's time is spent in dealing with allergic children. Some of this increase is due to improved diagnostic awareness of allergy on the part of doctors but it is also due, among other things, to the marked decrease in breast feeding by our modern mothers. . . . Seven times more infants develop atopic dermatitis from cow's milk than breast milk and 80% of these infants later develop respiratory allergies. . . . There is active sensitization in utero. . . . Because the human placenta is permeable to the passage of undigested food antigen, large quantities of a highly allergenic food eaten in the last trimester may give rise to active sensitization of the fetus. The infant may then manifest symptoms on first ingesting that food. . . . The first step in the program of prevention starts with the mother during the last trimester. The mother should be allowed no egg or chocolate and one pint of cooked milk a day. . . . Vitamin D and calcium are given as supplemental therapy. The mother is to practise a diversified feeding program, particularly of sensitizing foods, by eating small amounts of a variety of foods. Food cravings should not be satisfied. . . . Food excesses tend to increase allergic manifestations. Excessive eating of seasonal foods produces some of our most severe reactions. Some of these coincide with our holidays, such as eggs at Easter and nuts at Christmas.—J. E. Stroh, M.D., and J. W. Georges, M.D., *British Columbia Medical Journal,* March, 1959.

CLINICAL NOTES

RESERPINE-INDUCED GASTROINTESTINAL HEMORRHAGE

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It is well recognized that reserpine, the crystalline alkaloid of Rauwolfia serpentina, can produce such undesirable effects as mental depression or Parkinsonism. An equally severe, but less well known, complication is acute upper gastrointestinal hemorrhage. Some patients in whom this has occurred have had a previous ulcer history,[1] whereas others have not.[2] Hollister [2a] reports hematemesis in a patient given 25 mg. of reserpine intramuscularly and 9 mg. orally over a five-day period. There had been no history suggesting peptic ulcer, and x-ray studies revealed only a hiatal hernia and enlarged rugae, no ulceration.

Lesser amounts for longer periods can produce the same results. Gailitis and co-workers [2b] describe three cases of acute gastrointestinal bleeding resulting from administration of 0.5 to 1.0 mg. of reserpine per day for 6 to 24 months in patients without any previous gastrointestinal disturbance. "Barium swallow" in two cases showed no pathology, but autopsy in the third disclosed acute hemorrhagic gastritis. The development of a duodenal ulcer the first time reserpine therapy is given is also well documented.[3] The present case is reported in order to emphasize the rapidity with which reserpine can produce gastrointestinal bleeding.

Report of a Case

A 59-year-old man was admitted to the University of Minnesota Hospitals for the first time on Feb. 20, 1959, for hereditary chronic progressive chorea with mental deterioration (Huntington's chorea) of five to six years' duration. His only other illness of significance was an episode of biliary colic in 1953 associated with a nonfunctioning gallbladder seen on x-ray. There was no suggestion of gastric or duodenal pathology.

Physical examination revealed a well-developed man with generalized choreiform movements, obvious mental deterioration, and hyperactive deep tendon reflexes. The blood pressure was 160/95 mm. Hg and the pulse rate 100 per minute. Laboratory studies showed a hemoglobin level of 16.7 Gm. per 100 ml. with normal urinalysis findings and white blood cell count.

In order to decrease the involuntary movements, treatment with reserpine was begun according to the schedule outlined by Lazarte and co-workers.[4] On Feb. 23 the patient received 5 mg. of reserpine intravenously at 3:30 p. m. and 2 mg. orally at 10 p. m. At 5 o'clock the next morning he awoke with epigastric pains and during the next three hours vomited 500 to 600 ml. of material containing large amounts of fresh and altered blood. The pulse rate stabilized at 100 per minute, and the lowest blood pressure recorded was 130/65 mm. Hg. The reserpine therapy was discontinued, and gastric suction and intravenous administration of fluids and 1 unit of whole blood were started. Throughout the day a marked cutaneous flushing and a generalized uncontrollable shivering were noted. The entire abdomen, especially the epigastrium, was painful and tender to palpation, and the intestinal sounds were normal to hyperactive. Thirty-four hours after the initial vomiting, coffee-ground material could still be aspirated but milk feedings were now tolerated.

On Feb. 27 an upper gastrointestinal series revealed only a small hiatal hernia; no ulceration could be seen. Further laboratory studies showed a normal bleeding time, Lee-White clotting time, platelet count, and clot retraction. The prothrombin time was 16.6 seconds as compared to a control of 14.1. The blood urea nitrogen level was 23 mg. per 100 ml., and liver function tests showed a total serum bilirubin level of 0.5 mg. per 100 ml., negative cephalin-cholesterol findings, thymol turbidity of 4 units, and sulfobromophthalein (Bromsulfalein) retention of 10% in 45 minutes. Several days later a repeat sulfobromophthalein test showed a retention of 8% and the blood urea nitrogen level had fallen to 18 mg. per 100 ml.

The patient was placed on a bland diet and did well with no evidence of further bleeding. On March 11 the hemoglobin level was 16 Gm. per 100 ml. and a guaiac test showed the stool to be free of blood. Chlorpromazine therapy appeared to decrease the hyperkinesis somewhat.

Comment

Stimulation of gastric secretion is believed to be an important factor in the ability of reserpine to produce ulceration of the stomach and duodenal mucosa. In man it was found that 1 mg. of reserpine given intravenously produced a marked hyperchlorhydria which began in 30 minutes, persisted at least four hours, and was the same in ulcer and nonulcer patients.[5] Rider and co-workers [6] demonstrated hyperchlorhydria with oral doses as small as 0.5 mg.

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Studies utilizing dogs with Heidenhain's pouches[7] or patients who have had vagotomy or vagotomy and sympathectomy[6] suggest that reserpine increases gastric secretion by a peripheral action on the parasympathetic ganglions located in the wall of the stomach. A direct action on the parietal cells cannot be excluded. Kirsner,[8] in his review of the subject, cites evidence that neither adrenocortical steroids nor serotonin appear to play a role. Whether histamine is a factor is undecided.

Khirwadkar[9] claims to have demonstrated a striking prolongation of the clotting time by reserpine, both in vivo and in vitro. On the other hand, Haverback and co-workers[10] found no significant alteration of the bleeding time, blood-coagulation mechanisms, or capillary fragility in patients given reserpine.

In conclusion, it is most improbable that gastrointestinal bleeding in patients taking reserpine is simply a fortuitous occurrence. Considering the large number of patients who have been treated with the drug, however, *it is not a frequent complication.*

Summary

A case of acute upper gastrointestinal hemorrhage occurred within 24 hours of initiation of therapy with reserpine. The amount that the patient received was relatively large—5 mg. intravenously and 2 mg. orally.

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FOOTBALL INJURIES.—From 1947 through 1957, slightly more than 2000 injuries were observed among members of the football squad at Ohio State University. A series of 2000 injuries seems impressively large until we find that only 1 out of 3 was severe enough to cause the player to miss practice, and only 1 out of 80 required surgical correction. The surgical correction consisted primarily of suturing of lacerations, care of simple fractures, and splinting and casting of injured ligaments. Only a few major surgical procedures were required. . . . The time the members of the squad lost from school because of injuries was approximately equal to the time lost because of other illnesses. Similarly, the number of days spent in the hospital because of injury was approximately equal to, but somewhat less than, the number of days spent in the hospital because of illness. . . . In the 10 year period, 20 men were considered unfit to participate in football because of injuries, and 10 men were considered unfit for football because of medical reasons unrelated to injury. Of the 20 men ruled out of football because of injury, 8 had repeated minor head trauma and 6 had knee injury. . . . Minor head injuries are fairly common in football. Early return to play after a head injury often is followed by a repeated head injury. . . . Any head-injured player with prolonged unconsciousness or prolonged sequela or with any physical sign is hospitalized immediately for the usual observation and treatment. This type of head injury is rare in this 10 year experience. Only a few players have been hospitalized because of head injury, and only one had x-ray evidence of fracture. . . . The other potentially serious problem in football injuries is injury to the cervical spine. This occurs with the neck in flexion. It is extremely important that athletes be trained and conditioned to avoid flexion of the neck or ducking of the head while blocking, tackling or running.—R. Patton, M.D., Football Injuries in a "Big 10" University, *Postgraduate Medicine,* June, 1959.

CHOLESTASIS DUE TO PROCHLORPERAZINE

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During the past few years, jaundice has been reported rather frequently as a complication of several drugs of recent innovation, particularly those of the tranquilizer group. The clinical picture has been rather characteristic. The patient, when placed on therapy with the agent, in about 14 days develops fever, nausea, abdominal pain, muscle ache, and jaundice, in association with dark urine and light stools. The jaundice is usually gone within a few weeks but may continue for several months. Complete recovery is observed in most cases, but fatal agranulocytosis may occur. No particular treatment is indicated.

The laboratory data are those of an intrahepatic type of obstructive jaundice. The bilirubin level, particularly the direct fraction, is elevated, as are the alkaline phosphatase and cholesterol levels. There are no evidences of hepatocellular damage; cephalin flocculation is negative; and thymol turbidity, total serum protein level, and prothrombin time are all normal. The urine and stools contain both bile and urobilinogen. The histological picture in the liver is that of extrahepatic obstruction with bile stasis in the intracanalicular ducts, with periportal inflammatory cell infiltration in association with preservation of the normal lobular structure and with no evidence of hepatocellular damage or regeneration.

Although chlorpromazine is the chief offender among the tranquilizer drugs, arsphenamine, dinitrophenol, cinchophen, aurothioglucose, methyltestosterone, norethandrolone (Nilevar), thiouracil, para-aminosalicylic acid, sulfadiazine, and methimazole, also have been offenders.[1]

The result of a questionnaire [2] sent to 67 psychiatrists and mental hospitals is of interest. This inquiry on the occurrence of jaundice as a complication of the use of tranquilizing drugs indicated that among the 45 completed questionnaires 87 cases of jaundice had been reported. Available data indicate that 70 cases of chlorpromazine jaundice have occurred in about 15,000 patients treated. The sampled opinion suggested that the incidence of this complication was diminishing, perhaps as the result of greater caution in use of these drugs since it was first reported. In this inquiry three other phenothiazine derivatives were mentioned as offenders, namely, promazine (Sparine) hydrochloride, mepazine (Pacatal), and prochlorperazine (Compazine)—the latter in one instance only. There is, in the literature, only one actual report of jaundice as a complication of the use of prochlorperazine.[3] We now report another well-studied incidence of cholestasis following the use of this drug. This may help create an awareness of the possibility of cholestasis resulting from the use of this particular "tranquilizer." We wish to stress also the prognostic importance of fecal urobilinogen determinations during the course of this disorder.

Report of a Case

A woman, 49 years of age, was seen by one of us (J. R. D.) on Jan. 13, 1959. Results of the physical examination were negative. A history of recent nervous tension was elicited, and prochlorperazine, 5 mg., was given four times a day. This was the only medication received. After three weeks on this regimen she noted the onset of nausea, anorexia, and the development of a generalized pruritus. Her urine was observed to be very dark. She suspected there might be a relation between her medication and these symptoms, and she ceased taking prochlorperazine. A week later she had jaundice. At this time the direct bilirubin level was 4.75 mg. per 100 cc., and the indirect 1.47 mg. per 100 cc.

On admission to the Vanderbilt Hospital her jaundice was marked. There were no spider-type angiomas. The liver was just palpable, smooth, and moderately tender. The spleen was not palpable. There were no dilated veins over the abdominal wall, and no ascites. Results of the pelvic examination were negative. The thyroid was not palpable; no tumors were felt in either breast; the heart and lungs were normal.

The laboratory data were as follows: Urinalysis showed a pH of 5.5, a specific gravity of 1.025, occasional white blood cells, and was positive for bile and urobilinogen. The hematocrit was 44%; the white blood cell count was 7,775 per cubic millimeter, with differential count of 75% segmented forms. The sedimentation rate was 35 mm. per hour (Wintrobe) and the total eosinophil count 137 per cubic millimeter. The blood smear revealed normal numbers of red and white blood cells and platelets. The bleeding time was six minutes, the clotting time five minutes, and the clot retraction time two hours. The tourniquet test produced no

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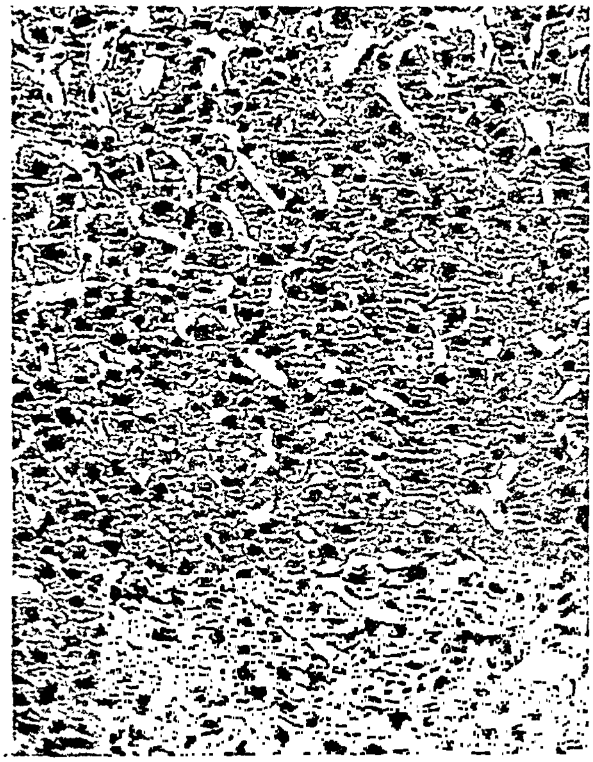
petechiae. Transaminase (serum) was 75 units. The nonprotein nitrogen level was 33 mg. per 100 cc., the blood sugar level 112 mg. per 100 cc., the serum protein level 6.7 Gm. per 100 cc., the albumin level 2.6 Gm. per 100 cc., the globulin level 2.6 Gm. per 100 cc., and alkaline phosphatase 7.1 Bodansky units. Cephalin flocculation was negative and thymol turbidity, 1 unit. The prothrombin time was 100% and the serum bilirubin level 1.9 mg. per 100 cc., direct, and 1.4 mg. per 100 cc., indirect. The cholesterol level was 350 mg. per 100 cc., and sulfobromophthalein (Bromsulfalein) · retention 37%. The stools were negative for blood, and urobilinogen was 260 Ehrlich units per 100 Gm. Heterophil agglutinations were negative. Values for the fragility test were as follows: initial hemolysis 0.33% NaCl, and complete hemolysis 0.30% NaCl. Chest x-ray, gallbladder series, gastrointestinal series, and electrocardiogram were all normal.



Liver aspiration biopsy, showing normal hepatocellular structure and evidence of cholestasis.

The patient was judged to have cholestasis due to prochlorperazine, and on March 14th a liver aspiration biopsy was performed by Dr. H. J. Shull. The biopsy revealed a characteristic pathological pattern of stasis in the biliary canaliculi without evidence of hepatocellular damage (see figure).

Her improvement was progressive, and the jaundice subsided promptly, as indicated in the table.

It was of considerable interest that the decrease in the bilirubin content of the serum was preceded by an observed increase in the quantitative fecal urobilinogen to 925 Ehrlich units per 100 Gm. This is confirmatory evidence of the mechanism for clearing the retained bilirubin, namely, by a mechanical overcoming of the cholestasis with discharge of the retained bilirubin into the biliary tract and consequently into the lumen of the intestine. There was never any indication of a hemolytic process.

Serum Bilirubin and Quantitative Fecal Levels Observed During Course of Treatment

Date	Serum Bilirubin Mg. per 100 Cc.		Fecal Urobilinogen, Ehrlich Units per 100 Gm.
	Direct	Indirect	
2/24/59	4.75	1.47	
3/ 2/59	1.9	1.4	260
3/ 4/59			182
3/ 7/59	1.5	1.3	
3/16/59	2.7	1.2	925
3/20/59	0.5	0.3	362
3/21/59			260
3/23/59	0.3	0.5	
3/24/59	0.4	0.4	

Summary

A patient developed classic cholestasis while taking prochlorperazine (Compazine). The pathological diagnosis was established by a liver aspiration biopsy. The following points are significant: 1. This is the second reported incidence of this complication in association with the use of this particular drug. 2. Chloroperazine must be used with the same care and caution given chlorpromazine and other similar chemical agents. 3. The mechanism of clearing of the jaundice is related to a mechanical discharge of the retained bilirubin into the biliary tract and the intestinal lumen. This may be measured by quantitative fecal urobilinogen determinations. 4. Daily quantitative fecal urobilinogen studies are a useful method of following the progress of the cholestasis and help predict the course of the disease.

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PULMONARY GRANULOMA DUE TO BRUCELLOSIS

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Brucellosis has long been known to involve the lungs in varied forms. Haden and Kyger[1] reviewed several hundred case records of brucellosis of the lung and reported the findings of seven cases in detail. The latter included pleural effusion, pneumonia, hilar and bronchovascular infiltration, and also pulmonary granuloma. The diagnosis of pulmonary brucellosis was made on the basis of clinical characteristics, a positive brucellin skin test, and the exclusion of other disease. The causative agent was not recovered from any of the patients reported. Greer[2] in 1956 surveyed 59 cases diagnosed as pulmonary brucellosis. In his series the findings were those of perihilar and peribronchial infiltration, patchy pneumonia, pleural effusion, empyema, and single granuloma. The diagnosis of pulmonary brucellosis was based on the history and physical findings, blood cultures, and skin, agglutination, and opsonocytophagic tests.

In 1956 Weed and co-workers[3] reported three cases of chronic localized pulmonary brucellosis. One of these cases had been previously reported in 1952.[4] All three cases were characterized by well-defined densities of the lung on roentgenographic examination. These lesions were surgically removed, and each proved to be a caseous granuloma from which Brucella suis was isolated by culture. The purpose of this paper is to report another case of proved chronic localized pulmonary brucellosis.

Report of a Case

The patient, a 42-year-old longshoreman, entered the West Side Veterans Administration Hospital on Nov. 20, 1957, with the complaint of pain in the lower part of the chest on the left side for the preceding four weeks. Except for a slight fever and malaise at the onset with a mild productive cough the patient had no other symptoms. At the time of admission the patient was afebrile and his pulse was 110 per minute. Physical signs of pleural fluid were present on the lower left side of the chest. The blood value determinations showed a hemoglobin concentration of 12 Gm. per 100 cc., with hematocrit 39%, and a white blood cell count of 18,100 per cubic millimeter, with 83% polymorphonuclear leukocytes, 11% lymphocytes, and 5% monocytes. X-ray examination revealed a large collection of fluid in the left side of the chest. Five hundred cubic centimeters of cloudy purulent material was removed, from which hemolytic streptococcus was grown. Sputum cultures also revealed hemolytic streptococcus. A pleural needle biopsy specimen was diagnosed as inflammatory tissue. The patient was treated with penicillin, and later a rib resection was performed for drainage of an encapsulated empyema. The patient had an excellent response and was discharged from the hospital on Jan. 29, 1958, with the drainage completely subsided.

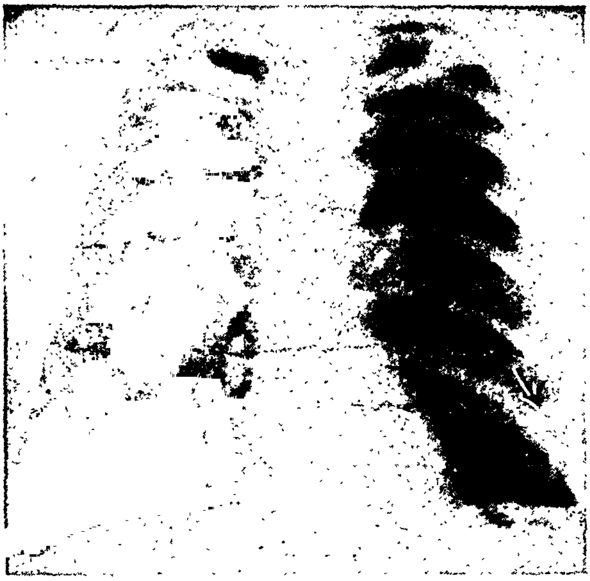

Fig. 1.—Roentgenogram made June 27, 1958, showing (*arrow*) nodular lesion of chest.

At the time of discharge from the hospital the chest x-ray still revealed considerable pleural thickening. He was examined at intervals and in March, 1958, a follow-up x-ray examination revealed a circumscribed density in the lower part of the left lung field. In June another film revealed the same well-defined round opacity, about 2 cm. in diameter (fig. 1). The density was thought to be in the lower lobe just below the major fissure. As the surrounding pleural reaction was subsiding the opacity became more evident. On July 25, 1958, persistence of the opacity was again observed roentgenographically. During this period the patient remained asymptomatic.

On Aug. 7, 1958, the patient was readmitted to the hospital. Results of coccidioidin, blastomycin, histoplasmin, and tuberculin skin tests were nega-

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tive. On Aug. 12, 1958, a wedge resection of the left lower lobe was performed with the removal of a firm round nodular mass.

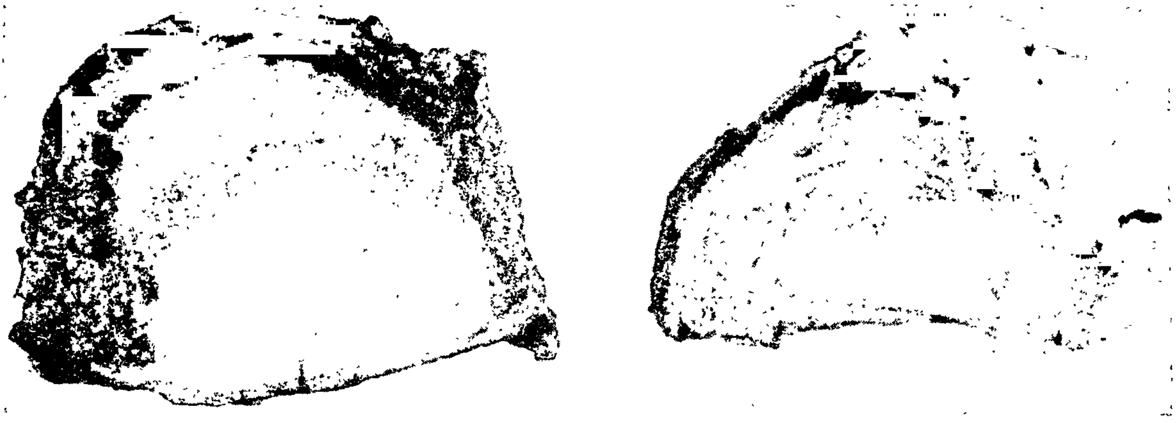

Fig. 2.—Cross section of resected nodule showing caseous necrosis and lamination.

Examination of a frozen section of the specimen revealed a granulomatous lesion. Gross examination of the removed mass showed lung tissue which was irregular in shape with a spherical firm nodule in its center. The latter measured 2 by 1.8 by 1.5 cm. The cut surface revealed a peripheral area of anthracosis and a central area of homogeneous firm white tissue with lamination and suggestive foci of calcification (fig. 2). Microscopic examination showed a large zone of caseous necrosis with hyalinization and focal calcification. At the periphery granulomatous inflammation was seen with an occasional giant cell (fig. 3). Stains for acid-fast bacilli and fungi gave negative results. Bacteriological study of the tissue showed Br. suis. Cultures for tuberculosis and fungi were negative. Results of Brucella agglutination tests done following surgery were negative on two occasions. The patient was discharged from the hospital on Sept. 3, 1958. He returned to his job as a longshoreman and has remained in excellent health.

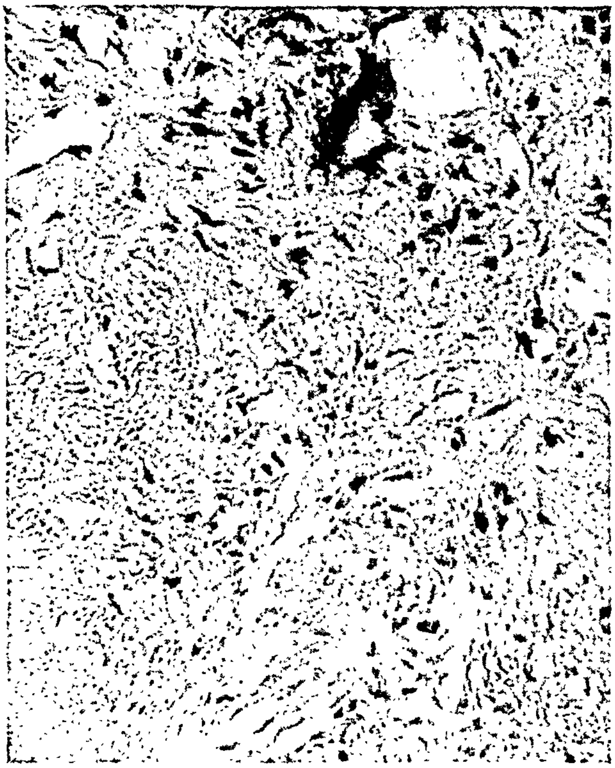

Fig. 3.—Microscopic section showing granulomatous inflammation with giant cells, and necrosis (×300).

Comment

We were impressed by the peculiar course of the disease in this patient. Originally an empyema was found, apparently caused by hemolytic streptococcus. After subsidence of the original infection the granulomatous lesion was discovered at x-ray examination. It is possible that the empyema was superimposed on an already present granulomatous lesion of the lung and that both processes had no relationship to each other. On the other hand, it is also feasible that this disease may have been a mixed infectious process with the streptococcus and Br. suis being the causative agents. However, this could not be proved since the previous culture was discarded after the hemolytic streptococcus was isolated. Quinn and Brown[5] reported a case of bacterial endocarditis with blood cultures positive for Br. abortus and alpha hemolytic streptococci (Streptococcus viridans).

As in the other three cases previously reported the diagnosis of Brucella granuloma was made only after bacteriological examination of the surgically removed tissues. It is coincidental to note that in these cases the causative organism was also Br. suis.

Weed and co-workers[4] have also emphasized the difficulty in establishing the diagnosis of offending organisms in chronic pulmonary infections and have pointed out that the majority of these lesions are caused by tubercle bacilli, fungi, or Brucella organisms. They also emphasized the difficulties encountered when histological findings alone are used to determine microbial etiology. Not infrequently the tissue reaction of brucellosis will simulate that of tuberculosis, and only bacteriological examination of the excised tissue will identify the causative organism.

The finding of granulomas in other organs than the lung has been recorded by various investigators. Barrett and Rickards[6] found granulomas due to brucellosis in the liver with focal calcification. Weed and co-workers[4] found noncaseous granulomas in the liver and hilar lymph nodes of the spleen in a case of brucellosis.

The negative results of the agglutination tests in our patient were not necessarily disturbing. As Weed and co-workers[1] pointed out, the granulomatous lesions are well encapsulated, thus keeping the antigen from the general circulation.

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COMMITTEE ON TOXICOLOGY

The danger of suffocation presented by discarded polyethylene garment bags and plastic dry cleaning bags used as improvised mattress or pillow covers has been, until recently, generally unrecognized as an accidental hazard for infants and small children. Over a year ago, concern was expressed in Europe over the possible danger of suffocation of small children who placed plastic bags over their heads while playing; however, the hazards of plastic garment bags used as improvised mattress or pillow covers and the ominously increasing number of accidental deaths attributed to them has only recently received widespread attention in the United States.

The Committee on Toxicology became aware of the problem in January, 1959, on receipt of a medical society notice of four deaths from plastic bags in children in a one-week period in Phoenix, Ariz. As part of its environmental health activities, the Committee immediately forwarded notices to large metropolitan and national public health agencies. Nationwide attention was directed to the problem after a report in The Journal. *In the meantime, various public health groups initiated independent investigations and warnings. In particular, the National Safety Council undertook a survey of state health departments for accident statistics; local and state health departments alerted poison control activities and issued public warnings; the United States Public Health Service launched a nationwide epidemiologic investigation.*

The following paper is a status report of the progress which has been made in the evaluation of this public health problem.

Bernard E. Conley, Ph.D., *Secretary.*

DANGER OF SUFFOCATION FROM PLASTIC BAGS

A distressing number of deaths by suffocation have been reported since the original article in The Journal (169:2021 [April 25] 1959) called attention to the danger of allowing small children to play with plastic bags. Infants and young children have suffocated when they became ensnared in thin polyethylene film such as that used by dry cleaners for garment bags. It has been claimed that an electrostatic charge, generated by friction from handling, causes the film to cling tightly to the nose and mouth. The child, enmeshed in the clinging film, is unable to free himself and suffocates. Tragedies have occurred while children were playing with the bags, usually after the bags have been pulled over their heads, and reportedly as the result of using the plastic film as a makeshift pillow case, mattress cover, or blanket protector.

Because of the recent publicity on this unrecognized hazard, various public agencies have made surveys to determine the seriousness of the problem. A National Safety Council survey of 48 state health departments revealed 20 reported deaths in 10 states due to suffocation from plastic materials from January to March, 1959. Four states reported a total of nine deaths during 1958. However, for several reasons, these figures do not represent the full extent of injury. Of the states responding, some reported for only a two-month period, some were not able to decode their records for such detailed information, and, in a few instances, news reports of suffocation had not yet been included in the public records. The majority of reported deaths occurred in infants 6 months old or younger. In the 16 cases in which age was recorded, 15 deaths involved infants up to 6 months, and 1 death occurred in a child over one-year-old. Further analysis of the records showed that plastic sheets were mentioned in seven deaths and plastic pillow cases in three deaths. In six cases in which plastic sheets were mentioned, the mother had used them to cover the mattress in the infant's crib.

A United States Public Health Department survey of the first six months of 1959 disclosed 61 reported fatalities attributed to plastic bag suffocation, 80% of whom were infants. The use of plastic dry cleaner's bags as waterproof sheets for babies' beds was found to be the principal cause of death. Intensive investigation of the deaths, including autopsy findings, occurring in a one-month period, revealed suffocation to be due to mechanical causes rather than to sudden overwhelming infection which sometimes causes the death of infants.

At the time of this report, approximately 70 deaths attributed to plastic bag suffocation have been reported from official and unofficial sources. Ten of these were intentional deaths in adults. It now appears that the early estimate of 100 deaths for 1959 may be a conservative estimate, if the following remedial measures do not become effective.

Means for publicizing the hazard and warning parents about the misuse of plastic bags are being intensively studied by various groups including the American Medical Association, the National Institute of Drycleaning, the National Safety Council, the United States Public Health Service, and the Society of the Plastics Industry, Inc. The American Medical Association and the National Safety Council have broadcast warnings over radio and television, and these stations have donated free time for spot announcements at various intervals. A national advertising campaign to educate the public on dangers of misusing plastic bags has been undertaken by the plastics industry. The National Institute of Drycleaning sent special notices to its 8,600 members, urging them to warn customers against giving plastic bags to children to play with. The Society of the Plastics Industry, Inc., has prepared an educational folder which illustrates the hazards and cautions against the misuse of plastic film. Various manufacturers of plastic garment bags are supplying warning labels or modifying garment bags in order to provide a safer product for dry cleaning establishments and their customers.

Legislators have also shown their concern. Bills requiring warning labels on plastic bags have been introduced into Congress and various state and local legislatures. Attempts to prohibit the use of plastic materials for garment bags have been defeated in legislative bodies in preference to requirements for warning labels. A sense of perspective is needed until all facts about the problem, including current research as to the mechanics of its causes, are fully evaluated. Despite current publicity of the hazards to children, public preference for plastic garment bags still prevails.

Plastic film is a popular and useful material for packaging and for providing a protective covering. It is found in the home on a variety of household articles. Clothing and accessories such as sweaters, hats, and handbags are often sold encased in thin plastic bags; plastic bags are used to package produce, drugstore items, toys, sporting goods, and a number of other products; dry cleaners also use the plastic bags as protective covers for finished garments.

Despite the sudden awareness of the potential danger to infants and children, the convenience and utility which plastic offers as a covering material suggests that it will continue to be used. It is therefore imperative that parents take the following precautions:

1. Do not give plastic bags or plastic film in any form to children to play with.
2. After plastic bags and wrappers have served their purpose, destroy them.
3. Do not use plastic film as slip covers for pillows and mattresses or as blanket protectors.

Should an emergency arise from the misuse of plastic film, the following steps are recommended:

1. If the child's breathing has stopped, the immediate need is to restore breathing. If possible, call out a neighbor or send for help. Ask that a fire department inhalator squad be summoned and that the nearest hospital be alerted.
2. Try to resuscitate the child, using the mouth-to-mouth technique recommended as the most effective method by the American Red Cross:
   a. Place the child on his back and extend the neck back. Put a towel or pillow under the shoulders so the head drops back.
   b. Lift the lower jaw up to assure an open airway.
   c. Place your other hand on the stomach to prevent its overinflation.
   d. Place your mouth over the child's mouth and nose and blow in. After each breath, turn your head to the side, take another breath, and blow in again. Repeat 12 to 20 times a minute.
3. If the child is suffering labored breathing, is stunned, or has difficulty in movement, rush him to the nearest hospital.

COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Cadmium Sulfide (Capsebon).—CdS.

Actions and Uses.—Cadmium sulfide, introduced in 1958, is used for the treatment of seborrheic dermatitis of the scalp (seborrhea capitis). Most investigators consider it of about the same order of effectiveness as selenium sulfide, although some clinical reports indicate that selenium sulfide is slightly more efficacious. Thus, cadmium sulfide affords temporary relief of excessive oiliness, scaling, and pruritus in a large percentage of patients with this common dermatosis. It should not, in any sense, be considered a cure for the disease but, rather, a means of controlling the symptoms of seborrhea as long as it is periodically applied.

Under ordinary conditions of use, cadmium sulfide is essentially nontoxic. When instilled into the conjunctival sac of dogs, the drug is much less irritating than selenium sulfide; no instances of chemical keratitis or conjunctivitis have been reported after its clinical use. As with any topically applied agent, contact dermatitis may occasionally develop. However, the incidence of sensitivity reactions and primary irritation to cadmium sulfide is quite low. The drug does not appear to be absorbed to any appreciable extent from the intact skin, and there are no reports of systemic toxicity after its topical administration. Cadmium sulfide does not cause either rebound oiliness or dryness of the hair and, if thoroughly rinsed from the scalp, does not discolor white or gray hair. It is free from objectionable odors.

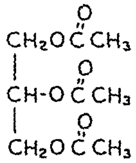
From the standpoint of safety and cosmetic acceptance, cadmium sulfide appears to compare favorably with selenium sulfide for the management of seborrheic dermatitis of the scalp.

Dosage.—Cadmium sulfide is administered topically in the form of a 1% suspension which is applied as a therapeutic shampoo. After wetting the scalp, 5 to 10 cc. of the suspension is applied by light massage to make a lather with which the hair is shampooed. After rinsing, the application is repeated. The second application should remain in contact with the scalp for 5 to 10 minutes and the head then thoroughly rinsed. For severe seborrhea, cadmium sulfide may be used every other day or twice weekly until improvement is noted. Thereafter, and in milder cases, weekly applications may be sufficient.

Preparations: suspension (topical) 1%.

Pitman-Moore Company, Division of Allied Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of cadmium sulfide.

Triacetin (Enzactin, Fungacetin).—Glyceryl triacetate.—The structural formula of triacetin may be represented as follows:



$$\begin{array}{l} CH_2O\overset{O}{\overset{\|}{C}}CH_3 \\ | \\ CH\text{-}O\overset{O}{\overset{\|}{C}}CH_3 \\ | \\ CH_2O\overset{O}{\overset{\|}{C}}CH_3 \end{array}$$

Actions and Uses.—Triacetin is an antimycotic agent introduced in 1956 for the topical treatment of superficial fungus infections of the skin. In concentrations of 0.1 to 0.25% it inhibits the growth, in vitro, of many of the species of Epidermophyton, Trichophyton, and Microsporum that commonly cause these infections; the more resistant Candida albicans is inhibited with higher concentrations. Its antifungal activity may be directly attributable to acetic acid, which is released from triacetin by a slow but sustained enzymatic hydrolysis by esterases. Such esterases, present in fungi themselves and also in human skin and serum, become inactive at a pH of about 4.0. Thus, the release of acid is self-limited and ceases when this degree of acidity has been produced. Attempts, in vitro, to induce resistance in fungi to triacetin have failed.

Although the antifungal activity of triacetin in vitro is well established, its effectiveness in vivo for the treatment of skin diseases caused by the aforementioned organisms has been questioned. It has been tried in infections caused by a variety of fungi involving the scalp, trunk, nails, groin, and feet. One clinician who has used the drug expresses the view that triacetin is of absolutely no value in these conditions; however, others apparently feel that it is of definite benefit, although its superiority to other drugs remains to be established. As with other fungistatic agents, tinea unguium responds only slowly, if at all. Triacetin has been employed, but without benefit, in blastomycosis of the skin. Results in superficial infections caused by C. albicans have been poor.

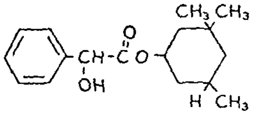
Triacetin does not irritate the skin. It has been applied to the ear canal and the vagina without ill-effect. In experimental studies, triacetin instilled into the conjunctival sac of rabbits daily for 15 days produced no evidence of conjunctival or corneal inflammation. Sensitization has not been reported. No effects attributable to systemic absorption after local application have appeared. It is odorless and stainless. The use of triacetin should be limited to the topical treatment of fungus infections of the skin. Although it produces little irritation, it probably should not be applied to acutely inflamed areas.

Dosage.—Triacetin is applied topically in concentrations of 25% or higher. Aerosols, ointments, powders, or solutions may be used. Methods and schedules of application do not differ significantly from those employed for other antifungal agents.

Preparations: aerosol (topical) 25%; ointment (topical) 25%; powder (topical) 33⅓%; liquid (topical) 30%.

Ayerst Laboratories, Division of American Home Products Corporation, cooperated by furnishing scientific data to aid in the evaluation of triacetin.

Cyclandelate (Cyclospasmol).—3,3,5-Trimethylcyclohexyl mandelate.—The structural formula of cyclandelate may be represented as follows:



Actions and Uses.—Cyclandelate, introduced in 1956, is an antispasmodic agent. Its action on smooth muscle closely resembles that of papaverine and may be classified as musculotropic, since there is assumed to be no specific biochemical antagonism to acetylcholine or to histamine. Spasmolytic activity has been demonstrated in vitro on a number of isolated tissues, including intestine, uterus, seminal vesicles, and gallbladder. It has about the same activity as papaverine toward spasm induced by the barium ion and slightly greater activity than papaverine toward that induced by histamine. It is only about 1/1,300 as active as atropine, however, in antagonizing acetylcholine-induced contractions. Cyclandelate partially suppresses the increased intestinal activity resulting from physostigmine injections, which may be considered evidence of antispasmodic activity in vivo. Several observations indicate that cyclandelate induces relaxation of vascular smooth muscle.

Studies on experimentally induced skeletal muscle necrosis and myocardial infarction indicate that, during the recovery period, the damaged areas are more vascular in animals treated with cyclandelate than in untreated animals. It is not clear whether this is due to vascular dilatation or to neoformation of blood vessels. Cyclandelate has no effect on cholesterol-induced atherosclerosis in rabbits. Oral administration in animals increases bleeding time but does not alter coagulation time.

In healthy human subjects, oral doses of 200 mg. of cyclandelate produce an increase in the digital sphygmic wave, total digital volume, and a slight but definite rise in skin temperature. The venous congestion test indicates an increase in flow per minute. Heart rate and blood pressure do not change appreciably. In normal subjects the effects of cyclandelate are detectable within 12 to 15 minutes after an oral dose, reach their maximum in about one and one-half hours, and have subsided within three hours.

Changes in obliterative vascular disease are qualitatively similar, but there may be considerable variation in the magnitude of the response from one patient to another. When studied in four patients with obliterative vascular disease who had been subjected to a unilateral lumbar gangliectomy, cyclandelate produced an increase in blood flow even in the denervated regions. The effects of a single dose in obliterative vascular disease may persist for four to six hours.

Early clinical reports of the use of cyclandelate in the treatment of peripheral vascular disease are favorable. Unfortunately, however, in the cases described, the patients were often subjected to other therapeutic measures as well, and true control observations were omitted. Cyclandelate is reported to have beneficial effects in obstructive vascular disease as well as in vasospastic conditions. Some investigators have reported better results in the former group of diseases than in the latter; this observation is difficult to explain. A varying percentage of patients with peripheral arteriosclerosis, diabetic angioses, thromboangiitis obliterans, acute thrombophlebitis, erythrocyanosis, local frostbite, Raynaud's disease, Raynaud's phenomenon, and vasospasm associated with neurological disorders have shown improvement after treatment with cyclandelate. Healing of refractory ulcers and relief of intermittent claudication are among the beneficial effects attributed to the drug. Results in acrocyanosis have been consistently poor.

Administration of cyclandelate to laboratory animals has produced no hematological abnormalities or other evidence of serious chronic toxicity.

Side-effects associated with clinical use of cyclandelate include flushing, tingling, dizziness, sweating, nausea, and headache. These are relatively infrequent at lower dose levels but occur in about one-third of the patients receiving total daily doses of 800 mg. or more. The sudden vasodilation, burning, and itching produced by nicotinic acid do not occur.

Cyclandelate may be used as an adjunctive agent in the treatment of peripheral vascular diseases. Although no vasodilator drug has proved consistently beneficial in these conditions, individual patients sometimes respond favorably. The relative efficacy of cyclandelate in comparison with other vasodilators is unknown, since there have been no systematic clinical investigations in which such a comparison was attempted.

Dosage.—Cyclandelate is administered orally. The usual dose is 100 mg. four times daily. Occasional patients may require larger doses, such as 200 mg. four times daily; in such instances annoying side-effects may occur, but they are usually mild and do not necessitate cessation of treatment.

Preparations: tablets 100 mg.

Ives-Cameron Company, Division of American Home Products Corporation, cooperated by furnishing scientific data to aid in the evaluation of cyclandelate.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The Council has authorized publication of the following report.

Philip L. White, Sc.D., *Secretary.*

EFFECT OF ALCOHOL ON THE LIVER

Gerald Klatskin, M.D., New Haven, Conn.

Alcohol is believed to play an important role in the pathogenesis of Laennec's cirrhosis and is known to potentiate the hepatotoxic effects of certain agents. Yet, paradoxically, in neither instance has it been established that alcohol exerts a direct effect on the liver. (In this report, the term alcohol refers to ethanol only.) The fact that alcohol has a caloric value of approximately 7 calories per gram and is capable of replacing isodynamic quantities of dietary carbohydrate in the support of growth[1] suggests that, in moderate amounts, it is a food rather than a poison. However, this does not exclude the possibility that, in excess, alcohol has a deleterious effect on the liver, as is the case with certain other foodstuffs. Indeed, the results of recent experimental studies[2] are consistent with this interpretation. The purpose of this report is to review briefly the evidence implicating alcohol as a factor in hepatic injury.

Relationship Between Chronic Alcoholism and Cirrhosis

The relationship between chronic alcoholism and cirrhosis has been recognized for over a century and is supported by autopsy evidence, indicating that the incidence of cirrhosis in alcoholics is at least six times as high as that in nonalcoholics and that the death rate from cirrhosis in many areas is closely correlated with the per capita consumption of alcoholic beverages.[3] Particularly impressive are the data showing the parallel decline in the death rates from chronic alcoholism and cirrhosis that occurred during the early years of the prohibition era in the United States.[4] Postmortem statistics probably underestimate the importance of alcohol as an etiological factor, since a reliable history of overindulgence may be difficult to obtain and often is omitted in clinical records and death certificates, particularly when cirrhosis is not the primary cause of death. This may account, at least in part, for the variable incidence of cirrhosis encountered in alcoholics examined post mortem, which has been reported to be as low as 1% in some series and as high as 25% in others.

On the basis of a careful appraisal of the autopsy data available in the literature up to 1941, Jolliffe and Jellinek[3] estimated that approximately 8% of chronic alcoholics ultimately develop cirrhosis. Even allowing for inaccuracies in the collection of these data, it is apparent that only a small fraction of heavy drinkers are subject to the disease. This suggests that there are differences in individual susceptibility to the effects of chronic alcoholism or that other associated factors play a significant role in the pathogenesis of cirrhosis. Although evidence bearing on the effects of malnutrition and other contributory factors is available in abundance, surprisingly little is known about the possible importance of differences in individual susceptibility. Unfortunately, the complexity of the exogenous factors to be considered is so great that it is not feasible to study this problem in man. However, it is noteworthy that in animal experiments, in which hereditary, environmental, and dietary factors are rigidly controlled, regimens designed to produce cirrhosis rarely affect all animals uniformly,[2] suggesting that endogenous factors may be important in determining whether or not cirrhosis develops.

Autopsy statistics on the incidence of chronic alcoholism in persons with cirrhosis show striking geographical differences.[5] To cite two extremes, the incidence was 86% in one series reported from Austria and only 2.5% in another reported from Turkey. Similar differences have been observed in various parts of the United States. Considering the multiplicity of factors that can give rise to cirrhosis, such differences are to be expected and reflect variations in the prevalence, not only of chronic alcoholism but also of other etiological factors in the populations selected for study. It is obvious, therefore, that, in evaluating the importance of alcohol as a factor in the pathogenesis of cirrhosis, greater weight must be given to the frequency with which chronic alcoholics develop cirrhosis than to the percentage of cirrhotic persons who are found to be alcoholic.

Despite the impressive body of evidence linking cirrhosis with chronic alcoholism, occasional investigators still question the relationship. An example is the relatively recent report of Voegtlin and his

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From the Department of Internal Medicine, Yale University School of Medicine.

associates [6] based on a clinical and laboratory study of 300 chronic alcoholics "from the better classes of society." Although a significant number of their subjects showed functional and physical abnormalities pointing to liver disease, the authors concluded that, while chronic alcoholism often produces hepatic dysfunction and fatty infiltration, it does not predispose a person to the development of cirrhosis. This interpretation was based on the erroneous assumption that the cirrhotic process is always irreversible and progressive and that the hepatic dysfunction it produces invariably follows a characteristic pattern, features that were not observed in their series. It is noteworthy that similar clinical investigations of alcoholics, which have included histological examination of liver biopsy material, have invariably shown a significant incidence of cirrhosis.[7] This illustrates the fallacy of drawing conclusions regarding hepatic morphology from data based solely on clinical and functional studies.

Although the evidence cited clearly establishes that there is a relationship between chronic alcoholism and cirrhosis, it gives no indication of the mechanism involved. To elucidate this aspect of the problem, numerous attempts have been made to produce cirrhosis in animals by feeding them alcohol. Almost without exception such experiments have been unsuccessful.[8] However, it has been found that alcohol enhances the hepatotoxic effects of agents like carbon tetrachloride,[9] chloroform,[10] and phosphorus [11] and increases the severity of the cirrhosis produced by certain deficient diets.[12] Accordingly, it has been suggested that the effect of alcohol on the liver is always an indirect one. Early investigators proposed that alcoholic beverages contained toxic contaminants, such as copper [13] or phosphorus,[14] or produced gastrointestinal changes that permitted the absorption of endogenous toxins.[15] This view had to be abandoned for lack of supporting evidence. More recently, interest has shifted to the possibility that the effects of alcohol are secondary to a nutritional disturbance.

Dietary Factors

At the present time it is generally believed that the development of cirrhosis in chronic alcoholics is the direct consequence of the faulty dietary habits that often accompany habitual drinking. According to this theory an excess of alcohol, by providing a large number of calories and by depressing the appetite in other ways, leads to a reduction in the consumption of food, and particularly of protein, resulting in a deficiency of lipotropic substances. The latter comprise a group of compounds including choline, a constituent of phospholipid; the amino acid, methionine, which provides an exogenous source of labile methyl groups needed for the endogenous synthesis of choline; and folic acid and cyanocobalamin (vitamin B_{12}), which, in some species at least, are essential for the *de novo* synthesis of methyl groups. A deficiency of these substances in the diet of animals leads to fatty infiltration of the liver, which in most species is followed ultimately by the development of cirrhosis.[16] Recent evidence [17] indicates that the accumulation of fat under these circumstances may be related to a reduction in the rate of fatty acid oxidation.

What connection there is between the deposition of fat and the ultimate development of fibrosis is still uncertain. It has been suggested that (1) the presence of fat interferes with the normal metabolic activities of the hepatic cell, leading ultimately to its death; (2) distention of the parenchyma with fat obstructs sinusoidal blood flow, resulting in relative anoxemia and cellular necrosis; (3) the regenerative activity of the fat-filled cells is diminished, so that the normally rapid replacement of worn-out cells is hindered, permitting fibrosis to occur; and (4) adjacent fat-filled cells tend to merge, forming large cysts that ultimately rupture into the sinusoids and bile ducts, leaving behind a collapsed capsule of condensed reticulum. However, not all forms of experimental fatty infiltration of the liver give rise to fibrosis, and not infrequently in human cirrhosis there is a marked discrepancy between the extent and the distribution of the fat and that of connective tissue. This has led some investigators to conclude that the two lesions are not causally related.[18]

It is becoming increasingly evident that the effects of protein deficiency on the liver are not limited to those dependent on an inadequate supply of choline and its precursors. Animals fed proteins containing insufficient amounts of threonine, lysine, and tryptophan develop a characteristic type of periportal fatty infiltration that is not abolished by choline.[19] Low-protein diets produce, in addition to the fatty infiltration expected, degenerative changes and foci of necrosis in the parenchyma not seen in pure choline deficiency.[20] This probably accounts for the fact that protein supplements are more effective than choline or methionine in the repair of experimental nutritional cirrhosis [21] and may be of significance in the pathogenesis of Laennec's cirrhosis.

Although a great deal has been written about the importance of vitamins in the treatment of liver disease, there is no conclusive evidence to indicate that deficiency of any of the vitamins, with the possible exception of folic acid and vitamin B_{12}, which, as previously indicated, appear to play a role in choline synthesis, is a factor in the pathogenesis of nutritional cirrhosis. Experiments purporting to show a specific effect of other members of the vitamin B complex [22] have either been lacking in pair-fed controls to exclude effects dependent on differences in caloric intake and growth rate or have been complicated by other deficiencies.

Regarding the pathogenesis of Laennec's cirrhosis in chronic alcoholics, certain similarities to experimentally induced nutritional cirrhosis are at once apparent. Moreover, a number of observations may be cited in support of the concept that the disease is dependent on an alcohol-induced dietary deficiency of lipotropic substances. Thus, it has been demonstrated that there is a high incidence of malnutrition in chronic alcoholics with cirrhosis and that high-protein diets are therapeutically effective,[23] even in the face of continued alcohol consumption.[24] Also, biopsy studies indicate that, as in the choline-deficient rat, the cirrhotic process begins as a simple fatty infiltration of the liver that progresses to the stage of fibrosis and that protein supplements facilitate the removal of such fat and prevent further progression of the fibrotic process.[24]

At autopsy, the liver usually exhibits a uniform pattern of connective tissue septa encircling small regenerating nodules and isolated islands of surviving parenchymal cells with varying degrees of fatty infiltration and degeneration. These features are characteristic of Laennec's cirrhosis, which is a lesion known to occur not only in association with chronic alcoholism but also in a variety of other conditions, many of which are accompanied by malnutrition. Although fatty infiltration is generally considered to be an essential feature, it may be absent late in the disease as a consequence of progressive inanition or in any other stage of the disease as a result of treatment. In its most widely understood sense, the term Laennec's cirrhosis implies a lesion in which fatty infiltration, due to any one of a number of causes including chronic alcoholism and malnutrition, appears to be the forerunner, if not the immediate cause, of diffuse hepatic fibrosis and nodule formation. However, the term is used by some to indicate any type of cirrhosis characterized by a fine diffuse fibrosis with nodule formation and by others to denote a form of liver disease due specifically to chronic alcoholism and/or malnutrition. No doubt much of the disagreement over the relative importance of alcohol and other factors in the etiology of Laennec's cirrhosis stems from this confusion in terminology.

Occasionally, alcoholics develop a coarsely nodular type of cirrhosis that closely resembles the postnecrotic cirrhosis seen during the recovery phase of massive or subacute hepatic necrosis due to the hepatitis virus and certain toxic agents. The question arises whether the lesion in such cases is of nutritional origin or is due to causes unrelated to chronic alcoholism. It is possible to produce similar lesions in rats by rigidly limiting their intake of the sulfhydryl-containing amino acids, tocopherol and selenium.[25] It is doubtful, however, that these very specific dietary conditions have ever been duplicated in man. Moreover, it has not been established that the human liver is susceptible to massive necrosis under such conditions; therefore, on the basis of present evidence, it would appear more likely that the postnecrotic form of cirrhosis seen occasionally in alcoholics is due to coincidental factors unrelated to chronic alcoholism or malnutrition.

Judging from the evidence cited, there can be little doubt that nutritional factors play an important role in the pathogenesis of Laennec's cirrhosis. However, there are a number of observations that appear to be inconsistent with the generally accepted view that the effects of alcohol on the liver in man are due solely to the reduction in food consumption that often accompanies excessive drinking. These may be briefly summarized as follows: 1. Alcoholics occasionally develop cirrhosis despite an apparently adequate dietary intake; conversely, patients with sprue, anorexia nervosa, and a variety of other wasting diseases accompanied by severe malnutrition rarely do. 2. The inflammatory, necrotic, and degenerative changes, including the presence of Mallory hyaline bodies, so characteristic of active cirrhosis in the alcoholic, are not seen in experimental nutritional cirrhosis. 3. In contrast to the relatively benign character of the lesion in protein-deficient animals, the fatty infiltration and degenerative lesions that occur in the liver of chronic alcoholics occasionally give rise to overt hepatic failure and may cause death, even in the absence of hepatic fibrosis.[26] 4. Significant improvement in the clinical, functional, and histological status of the liver has been observed in persons with cirrhosis after withdrawal of alcohol and the administration of diets considered suboptimal by current therapeutic standards.[27] In short-term studies similar improvement has been observed in subjects receiving diets virtually devoid of protein. Discrepancies such as these suggest that the effects of alcohol on the liver may not be limited to those dependent on a reduction in food consumption.

Recent experimental studies indicate that, in the rat at least, alcohol tends to create a deficiency of choline by reducing the intake of food, by adding nonprotein calories to the diet, and by increasing the choline requirement via a mechanism independent of food consumption or caloric intake.[2] Since the administration of alcohol in such animals leads to an immediate decrease in food consumption that is calorically equivalent to the amount of alcohol ingested, this effect would appear to be a normal response to the homeostatic mechanism for the maintenance of a constant caloric intake rather than a manifestation of an alcohol-induced gastrointestinal disturbance leading to pathological anorexia. Assuming that the same mechanism is operative in man, this may account for the discrepancy between the inadequacy of the diet in many chronic alcoholics and their apparent failure to lose weight. Considering the fact that a heavy drinker may consume between 1,000 and 2,000 calories a day in the form of alcohol, it is not surprising that he is able to maintain his weight and satisfy his appetite, despite a dwindling food intake. Obviously, the maintenance of an adequate caloric intake under such circumstances is made at the expense of essential nutriments, including proteins and vitamins, so that specific nutritional deficiencies may develop despite the absence of weight loss. However, long-continued drinking ultimately produces a pathological type of anorexia that leads to a reduction in total caloric intake and overt signs of undernutrition.

The experiments cited have established the important principle that the choline requirement varies directly with the caloric intake. Hence, if the diet is marginal in lipotropic activity, the mere addition of nonprotein calories, whether they be derived from alcohol or from carbohydrate, will induce a relative deficiency of choline. This may be one of reasons why cirrhosis is more common in alcoholics than in patients with chronic wasting diseases, in whom the diet may be equally deficient in protein, but whose caloric intake is significantly lower. Also noteworthy in this connection is the fact that in areas of the world where cirrhosis of presumed nutritional origin is prevalent, the native diet is deficient in protein but usually contains an abundance of calories in the form of carbohydrate.

Under appropriately controlled conditions it can be demonstrated that, in the rat at least, alcohol increases the choline requirement in still another way unrelated to changes in food consumption or the caloric intake.[2a] Quantitatively this effect appears to be even more important than the others. Nothing is known about the mechanism involved, but it has been suggested [28] that choline may be a factor in the metabolism of acetyl coenzyme A and, hence, may be required in greater amounts when alcohol is oxidized to acetate.

It is important to bear in mind that the increase in the choline requirement induced by alcohol cannot be demonstrated experimentally unless the diet is marginal in its content of lipotropic substances, resulting in an overt deficiency. This suggests that the alcohol effect is readily abolished by small amounts of protein or choline in excess of the minimum required to maintain the fat content of the liver at a normal level. This fact has been confirmed experimentally,[2a] which probably accounts for the observation that alcohol has no deleterious effects on the liver when administered to persons with cirrhosis receiving a high-protein diet.[24]

Recently it has been reported that cirrhotic persons with a daily protein intake of as little as 25 to 65 Gm. suffered no ill-effects when given alcohol in amounts equivalent to one-half pint of whiskey daily for two to four weeks.[29] Indeed, the authors were so impressed with the salutary effects of alcohol on the mental status and appetite of their patients that they endorsed its use in the treatment of alcoholics with cirrhosis!

This type of study is difficult to interpret and does not necessarily establish that alcohol is innocuous in chronic alcoholics with cirrhosis. First, six of the seven patients studied were not investigated until icterus or ascites, or both, had improved, presumably as a result of treatment. This raises a question regarding the possible sustained effects of protein stored during this preliminary period. Second, although liver function and morphology either improved or showed no change, the possibility that the rate of improvement was slowed or delayed was not excluded, particularly since no data are given on the rate of recovery before the experiment was started. Third, no account is taken of the possible benefits derived from the decrease in physical activity imposed by hospitalization, a factor that could conceivably have obscured the effects of alcohol. Fourth, five of the subjects received 60 to 65 Gm. of protein daily, an amount adequate to promote recovery in most cirrhotics,[27] and possibly significantly in excess of the minimum required to obscure the effects of alcohol. Fifth, the authors state that, at the beginning of the experiment, anorexia was so severe that it was difficult to maintain a constant intake of food but that there was rapid improvement when alcohol was administered. In the absence of any data to the contrary, this suggests that the protein intake may have increased, thus protecting the patient against the alcohol effect. Finally, in subjects drinking the amounts of alcohol used in this experiment, signs of liver disease, whether they be due to nutritional or other factors, do not appear for a number of years, so that the period of observation of two to four weeks may have been inadequate.

Enzymatic Activities of the Liver

In addition to the changes alcohol may evoke by inducing a nutritional deficiency, it may affect the liver in other subtle ways. One of these relates to its possible interference with some of the enzymatic activities of the liver. It has been demonstrated that, in yeast suspensions, alcohol blocks the reduction of the cytochromes, a group of important iron-containing cytoplasmic heme proteins that serve an essential role as electron carriers in the complicated chain of enzymatic reactions involved in oxidation.[30] Similarly, it has been reported that alcohol may reduce the activity of the citric acid cycle in the liver.[31] The evidence for this is the observation that, after the administration of alcohol, there is an increase in the lactate and acetate and a decrease in the pyruvate, alpha-ketoglutarate, and citrate content of the hepatic venous blood.

In its oxidation alcohol undergoes rapid successive dehydrogenations to acetaldehyde and acetate, enzymatic reactions involving the transfer of hydrogen and electrons via the coenzyme diphosphopyridine nucleotide (DPN), which serves as a carrier and is reduced in the process. In the report cited the author suggests that pyruvic acid is the hydrogen acceptor in this reaction yielding lactic acid and that the activity of the citric acid cycle in the liver may be depressed temporarily as a consequence of the rapid removal of pyruvic acid and the accumulation of reduced DPN.[31] Moreover, he postulates that this may reduce the amount of adenosinetriphosphate (ATP) generated in the cycle; hence, it may inhibit ATP-dependent enzymatic reactions, which over a prolonged period might result in a cellular injury. Recently the activity of still another enzyme in the liver, glutamic pyruvic transaminase, has been found to be decreased under the influence of alcohol.[32] The aforementioned enzymatic defects do not necessarily constitute a complete inventory of all those that may occur. Since this aspect of the alcohol problem has received scant attention, further investigation may reveal other abnormalities of equal or even greater importance. Whether or not alcohol-induced aberrations in enzyme activity play a role in the pathogenesis of liver disease is still problematical. Nevertheless, these observations suggest new avenues of investigation and illustrate the important point that, in the metabolism of an apparently innocuous substance like alcohol, there may be unexpected and possibly deleterious side-effects.

Possible Role of Infection

Certain features of the cirrhosis encountered in chronic alcoholics are not readily explained on the basis of a nutritional or metabolic defect and are not reproducible in experimental animals maintained on deficient diets and a high intake of alcohol. Of particular interest in this connection are the manifestations exhibited in the florid form of the disease.[33] These include a progressive downhill course, signs of hepatic failure that are refractory to dietary and other forms of treatment, and the presence in the liver of extensive necrotic, degenerative, and inflammatory lesions engrafted on an underlying fatty infiltration and/or cirrhosis. Usually the onset is insidious after a prolonged period of heavy drinking and dietary restriction, but occasionally it is acute.

Although fever and leukocytosis are common, overt signs of intercurrent extrahepatic infection are unusual. The features described suggest the possibility that the liver itself may be the site of infection. Occasionally bacteria have been demonstrated in the liver [34] and blood [35] of such patients. However, the more frequent finding of negative cultures and the ineffectiveness of antibiotic therapy in most cases of florid cirrhosis make it unlikely that bacterial infections play an important role in this disease. Moreover, it is highly probable that the occasional occurrence of bacteria in the liver is the consequence rather than the cause of the underlying hepatic disease and is indicative of a breakdown of the important defense mechanism in the liver for the destruction of organisms that gain access to the blood.

Another more interesting possibility is that the hepatitis virus is implicated, and that chronic alcoholism either increases the susceptibility to intercurrent infections or activates latent infections in carriers. Admittedly, the lesions in florid cirrhosis do not resemble those of classic acute vital hepatitis. However, the possibility cannot be excluded that the presence of antecedent hepatic injury related to chronic alcoholism modifies the morphologic manifestations of such infections. Unfortunately, no attempts have been made to demonstrate the virus in alcoholics with cirrhosis by means of human transmission experiments, the only method available at the present time. However, it is noteworthy that, in an investigation of apparently healthy blood donors thought to be responsible for hepatitis infections in recipients, four of the five who proved to be carriers by transmission experiment were excessive drinkers, and three investigated by liver biopsy showed either cirrhosis or less extensive hepatic fibrosis and inflammation.[36] Obviously, further studies of this type are needed to establish whether or not the hepatitis virus is responsible for any of the clinical or pathological manifestations of cirrhosis in alcoholics.

As previously noted, the old theory, that the absorption of toxins from the gastrointestinal tract under the influence of alcohol is a factor in the pathogenesis of cirrhosis, had to be abandoned for lack of supporting evidence. However, it has been revived as a consequence of recent reports indicating that broad-spectrum antibiotics which suppress the intestinal flora delay the appearance of hepatic necrosis in animals maintained on necrogenic diets [37] and prevent the development of hepatic fibrosis in choline-deficient animals.[38] As provocative as these observations are, they do not prove that toxic substances from the intestinal tract injure the liver, since in neither of these experiments was the possibility excluded that the antibiotics used contained a protective factor or that suppression of the intestinal flora deprived the animal of protective substances of bacterial origin.

Summary

A review of the evidence indicates that chronic alcoholism is an important, but by no means the only, etiological factor in the pathogenesis of Laennec's cirrhosis and that, whereas the malnutrition associated with excessive drinking undoubtedly accounts for many of the effects of alcohol on the liver, other as yet unidentified mechanisms may be involved.

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MEDICINE AT WORK

- ✓ **APPROACH TO AGING . . .**
  - *. . . in a Rural Area*
  - *. . . in a Metropolis*
  - *. . . at National Level*
- *Hospital Planning*
- *¿Habla Español, Doctor?*
- *Drag & Sag End in Texas*
- *Cementing World Medicine*
- *An Oriental Tale*

Story of Tao Koo

Author and physician Thomas A. Dooley, from his "little hospital on stilts" in the northern mountains of Laos, recounts this tale of compassion and survival:

"A 7-year-old tribes-boy named Tao Koo had a scorching fever and diarrhea. Within two weeks the child developed a bed sore. Within a month this had spread until all the flesh from his lower back and buttocks had sloughed off. He shrank and withered until he was just the shadow of a child. Finally the father brought him to us in Muong Sing, a three-day walk.

"Earl Rhine and Dwight Davis [Dr. Dooley's assistants] immediately took that little urinoid glob of flesh and washed him with all the tenderness they could muster. With the hearts of men, the hands of women, and a little of the mystery of God they gently scrubbed his sores, treated and dressed them. They rigged a special bed for him, tying balloons across the cross-bars. They pasted pictures to the wall alongside it. They gave him a coloring book and a squeaking rabbit.

"On the few days that we have sunlight they bring his bed outside. The dressings are removed. This wistful little lad, God's compromise between flower and dung, an interval between birth and death, once again began to live. He began to smile. Sores are closing up. He is happy."

For a view of medicine on the other side of the bamboo curtain, see p. 1685.

Rural Attack on Aging—A First Step

Doctors Provide the Spark That Sets a Town to Thinking

Big cities may be the heart of a nation, but it is in the vast throb of rural America that the complex problem of aging pulsates as a personal matter. Here there is no hustle and bustle of a concentrated population to engulf that problem as one of many—perhaps to shelve it dispassionately. The following report shows a neighbor-to-neighbor concern for the difficulties encountered when, say, one small-industry worker retires, or when a graying farmer no longer can take the daily routine of managing a dairy herd.

In facilities for the aged Wisconsin's Fond du Lac County (pop. 75,000) is probably more fortunate than most rural areas. Two religious groups operate homes for the elderly, and the entire area takes pride in the brand-new county home. There are also two proprietary nursing homes.

But the residents of Fond du Lac County know it takes more than institutions to ease the pressures generated by a rapidly expanding segment of elderly citizens. Yes, you would expect to find ministers acquainted with the needs and hopes of the elderly, but this same familiarity also extends to the slender and sprightly manager of the telephone exchange, to the friendly but reserved president of one of its banks, and to the community's teachers, attorneys, and clubwomen.

This awareness is no accident. Fond du Lac's people have all the usual human regard for the problems of a neighbor, but it took positive action by the county medical society to acquaint them with the unlimited challenge of caring for their oldsters and to offer a forum for the ideas and opinions of others.

Banker, physician, businessman: Rural Fond du Lac County in Wisconsin hopes to improve the lot of its aged through widespread cooperative effort. From left are W. A. Sanders, Dr. A. M. Hutter, and O. C. Claus.

That forum was called a Community Roundtable Conference, and neither the snow nor the cold of a day last December kept businessmen and labor leaders, nurses and hospital administra-

Three-Way Split

Nursing-home facilities for Wisconsin's chronically ill and aged are almost equally divided among proprietary, nonprofit, and governmental operation, according to the Division on Aging of the State Medical Society of Wisconsin.

In 1958, with a total of 18,129 residing in these homes, 38% were cared for in proprietary facilities, 30% in nonprofit homes, and 32% in governmental institutions.

tors, physicians and attorneys, and welfare workers and clergymen from attending.

Enthusiasm for the project radiates from Dr. A. M. Hutter, a Fond du Lac internist and chairman of the county society's committee on aging, as he sits at his desk and tells you about it. On the wall is a wartime photograph of himself in Naval uniform standing self-consciously beside a Yule-decorated dispensary refrigerator bearing a large sign emblazoned "Dr. Hutter's Penicillin Tree."

"Those people were not only ready for us," he says, "in some cases they were way ahead of us. I opened the conference with an outline of some of the basic medical and psychological problems faced by many of our elderly people. Then the other fellows told of the kind of thing they meet up with in treating the aged."

The "other fellows" are four local colleagues—Dr. D. W. McCormick, an orthopedic surgeon; Dr. H. K. Gugh, a urologist; Dr. James Habermann, a general practitioner; and Dr. William Wojta, an ophthalmologist.

At First—Hesitation

As the professional men finish, lay participants tell the conference what they know of the difficulties encountered by older people, and of some of the successes and failures that have marked efforts to help.

Some are hesitant at first. Among them is O. C. Claus, district manager in Fond du Lac for the Wisconsin Telephone Company. But, as he listens, Claus comes to realize that a program with which he has an intimate connection is a perfect case in point.

As a veteran employee of the phone company, Claus became eligible, after 21 years of service, to join a nationwide organization known as the Telephone Pioneers (see Medicine at Work, The Journal, March 21, 1959). Claus did join and immersed himself in the fellowship of the group. Later, as head of the local chapter, he became disturbed by the obvious difficulties of some of the men when it came time for their retirement. Not too far from retirement himself, he decided the Pioneers could help.

Under his direction a new subdivision of the group was formed. Called the Life Member Club, it is open to all retired telephone employees. Claus says, "They meet once a month in the conference room here at the office. After the meeting they go downtown for lunch. Each man pays for his own, too, and they have a pretty good time."

Although the group got off to a mild beginning even Claus is surprised by the momentum it has picked up. "First they decided to have a Christmas party. They planned it carefully and put it on themselves. When it turned out to be a success, they decided to take on more projects. The next thing was a picnic and right now it's a hobby show that is going to be held right here in the building. It's surprising how even a minor sort of activity like this adds purpose to life, once you've retired."

Frame of Reference

Others view the difficulties of aging in terms of their own experience. Two clergymen—Father Henry Maurer of St. Mary's Catholic church, and Rev. Karl Koehler of the Evangelical and Reformed Church of Peace—stress the importance of religious life to the aged. At the Community Roundtable Conference last December they urged the establishment of church-sponsored social groups for the aged and expressed the conviction that peace of mind and heart are especially necessary to the well-being of the elderly person.

True, all this interest and concern has not really solved anything yet in Fond du Lac County. No revolution in community thinking has yet taken place. No well-rounded, carefully planned, multiphased approach to the many needs of the county's aged has yet appeared. But Dr. Hutter feels today that an important beginning has been made. He calls the Roundtable Conference a success and advocates extension of the idea. He says, "The big need now is for education in this field—education and leadership. We've got to educate our people to the nature and extent of the problems faced by those over 65, and we have to educate our physicians to assume roles of leadership in their own communities."

If any physician in Wisconsin is in a position to do this it is Dr. Hutter, who wears two hats in the field of aging. He not only is chairman of the Fond du Lac County medical society's committee on aging, but he also heads the Aging Division of the State Medical Society of Wisconsin. And it is significant that, having tested the idea on his home ground, Dr. Hutter recommends the

Community Roundtable Conference as a good device for organizing interest in the problems of oldsters in any area.

What is next in Fond du Lac's effort to aid the aging? Well, if county chairman Hutter takes the advice of state chairman Hutter, it might be any one of a number of things—speaker services for schools, development of a retirement-preparation program for industry, or a countywide survey of the needs, services, and facilities for aging and long-term patients.

Medical societies in two other counties, Dane and Sheboygan, have already accepted the survey suggestion. Working with their respective welfare councils, the societies have guided county residents in comprehensive studies of this type.

Other Places, Other Things

Medical societies in other parts of Wisconsin, urged by the state society's Division on Aging, have also attempted programs of their own:

—The Brown County medical society is giving support to a community project in Green Bay to improve the lot of the chronically ill in nursing homes.

—The Racine County medical society is providing medical personnel to conduct preretirement programs for industries located in its area.

—The Marathon County medical society sponsors radio and television programs on the subject of aging for listeners and viewers in or near Wausau.

Dr. Hutter thinks those interested in helping the aged may be unintentionally scaring off prospective stalwarts by the introduction that many of them get. He says, "Don't start off by taking them on a tour of the geriatrics ward of the local hospital, because they'll only see patients who never had a chance at rehabilitation. Those patients do need good care and deserve it, but the long-range solution is to train the younger person for old age—to understand diet, positive health measures, and freedom from emotional conflict."

Some measure of the increasing awareness of broadly human needs of the elderly in Fond du Lac County is indicated by the feelings of two businessmen. Listen to Mr. W. A. Sanders, president of the National Exchange Bank: "It comes as a jolt when we comprehend what it really means when we say that almost 10% of the people in Wisconsin today are 65 or over."

Or Mr. Claus of the telephone company: "It isn't enough to give a man a party, a pension, a pat on the back, and best wishes for a long and happy life. A man needs to feel he isn't being cut off from the people with whom he's spent a big part of his life."

Rx for Housing

Three ways to help elderly persons finance adequate housing without using any new form of government help have been suggested by a New York banker. Speaking to physicians and other participants at the University of Michigan's 12th annual Conference on Aging, June 23, Harry Held made these proposals:

1. Offer life and health insurance programs to the elderly which would insure their ability to make mortgage payments in the event of sickness or death of one spouse.
2. Give middle-aged and elderly home buyers a chance to make higher mortgage payments during the initial period of home ownership, with tapering monthly installments for advancing years.
3. Provide those covered by pension plans with an option to use part of their pension credit as the down payment on retirement housing.

Held believes that, on the basis of present life expectancies, the final age limit on which mortgages might be made could reasonably be increased to 75 or even 80 years of age for home buyers aged 65 and over.

A village within a city—The Presbyterian Home in Evanston, Ill., recently announced it would turn its 43-acre site into a community of cottages, duplexes, apartments, and a convalescent home for the elderly. Completion will raise the home's population to 600 from its present 165. Present facilities include a hospital.

An Asset—Not a Liability

Healthier Senior Citizens Can Solve Their Own Problems

"If we can—through research—find ways for older people to remain healthier for a longer period of time . . . then we will see our aging population not as a problem or series of problems, but as a magnificent asset."

This was the optimistic picture painted by Rep. John E. Fogarty (D., R. I.) at the first national conference of the Joint Council for the Health Care of the Aged, held June 12-14 in Washington, D. C.

He based his bright hope on results expected from continued and increased efforts in research sponsored by both the National Institutes of Health and private institutions. He advocated extending the search beyond the borders of this country. Representative Fogarty said, "Some nations may already be ahead of us in research on aging. In Sweden, for example, they were carrying out farsighted programs to aid their older persons some years before aging attracted interest in this country. It would be to our benefit to learn more of what other nations are doing."

More than 450 physicians, dentists, hospital and nursing-home personnel, and others interested in the aged attended the conference. The joint council—sponsor of the affair—includes in its membership the American Dental Association, the American Hospital Association, the American Medical Association, and the American Nursing Home Association.

Whatever the values of future clinical research, warned Dr. Ewald W. Busse, director of the Center for the Study of Aging at Duke University, it would be a mistake to wait for all the results. He said, "We are in an interim period; and while we are waiting for the results to appear we must fill in the gaps and move in some positive direction."

Governor Robert Meyner (upper right) of New Jersey was among more than 35 persons invited to address the first national conference of the Joint Council on the Health Care of the Aged.

Get a Second Career

One way to beat compulsory retirement at 65 is to embark on a second career.

This solution is offered to those who dread the inactivity of retirement by a 75-year-old California woman who is a walking advertisement for her own formula.

In 1944 Ethel Percy Andrus, Ph.D., voluntarily retired as a high school principal in Los Angeles, and since then she has founded two national organizations, become editor of two magazines, and traveled extensively. Her second career is in the field of counseling the aged, and the keynote of her advice is action. In a recent *New York Times* interview Dr. Andrus urged her retired peers to do things, be of service to others, and see the world.

She is president of both the National Retired Teachers' Association and an affiliate, the American Association of Retired Persons, and she founded both of them. Dr. Leonard Larson, chairman of the A. M. A. Board of Trustees, in a recent letter to Rep. Wilbur D. Mills, chairman of the House Ways and Means Committee, praised the hospital and surgical insurance coverage provided by the AARP for its more than 300,000 members.

The group has also built a home for retired teachers in California, and it arranges leisurely European tours for elderly persons with an urge to see the world.

The plan of immediate action advocated by Dr. Busse is a series of small conferences bringing together investigators, clinicians, and "action leaders." Such teams, he believes, would have the responsibility of working out plans of action and explanations and would make recommendations to the joint council, the government, and the public.

Other speakers at the Washington session outlined problems, suggested solutions, and told of their failures and their successes in dealing with all facets of the care of the aged. These are some selected comments:

Health Insurance—"Prophecy is always hazardous, but it is possible on the basis of past performance and a knowledge of current developments to project an estimate of future expansion of voluntary health insurance among the aged, assuming no interference or preemption by government. If reasonable allowance is made for factors that are improving the growth rate, a good case can be made for predicting that 65% of the aged who need and want voluntary health insurance will be insured by 1960, 80% by 1965, and over 90% by 1970."

E. J. Faulkner, Chairman
Health Insurance Council

Dental Care—"Finding dental conditions which need attention, and providing immediate treatment, will help the homebound or chronically ill patient psychologically and medically. When oral conditions are corrected the patient will have a better opportunity to handle food, improved esthetic appearance—leaving remaining energies of the patient to conquer or partly override his chronic medical disabilities."

Dr. Leonard Reichman
Adjunct, Dental Division
Albert Einstein Medical Center

Attitudes—"Unfortunately, the concept of aging as expressed in earlier days was not a very joyful one. These pronouncements have done much to create the unrealistic gloomy backdrop upon which the problems of aging are grafted today. Is it not now understandable why everyone, including the physician, has had his thinking tinted by this somber mood?"

Dr. Frederick C. Swartz, Chairman
A. M. A. Committee on Aging

Rehabilitation—"When the value and contribution of restorative services in hospitals is being evaluated, it is important that both sides of the coin should be examined. That is, not only the operating cost but also the financial gains achieved by shorter hospitalization, cheaper nursing care, economical use of available beds, and decreased welfare expenditures. There are also many intangibles such as the elimination of depressive states, preservation of family structure, and improvement of the professional atmosphere in hospitals."

Dr. Michael M. Dasco
Goldwater Memorial Hospital
New York City

Home Care—"Blue Cross participation would help to hasten the development of organized home-care programs. Heretofore, these programs have been financed mainly by grants and private or tax funds on a time-limited basis. In most Associated Hospital Service (N. Y.) member hospitals more than 50% of the patients are subscribers. In some hospitals 80% are subscribers. Therefore, payment by AHS for home care used by subscribers would help to stabilize the financing of organized home care."

Maria Phaneuf, R.N.
Associated Hospital Service

Use of Facilities—"Some relatives feel that releasing the patient to a nursing home is evidence that the hospital no longer believes the patient is treatable. Others feel the care in the hospital is more adequate. Some feel that they will have to bear all the cost of care in a nursing home. These misconceptions emphasize the need for the preparation of the relative for the patient's release. The patients too must be prepared for their leaving, since many have become 'institutionalized' and fear to depart."

Drs. Cecil Wittson and Jackson Smith
University of Nebraska College of
Medicine

Poor Housing and the Aged

Eight million Americans 65 or more years of age are forced by financial circumstances to live in dilapidated quarters of our communities, under conditions which promote mental and physical illness and crippling disabilities.

So says Wilma Donahue, Ph.D., who heads the University of Michigan's Division on Gerontology. She testified recently before a U. S. Senate subcommittee on problems of the aged.

Dr. Donahue said this is a problem that must be faced by the communities themselves, since only 10% of retiring workers can be expected to leave their home towns. She advocated a larger supply of good housing and well-planned developments to serve older people, who usually move in with their children "only when forced to do so because of long-term disabling illness, absence of income, or devastating loneliness brought on by the loss of spouses or other social contacts."

Dr. Donahue did see one bright spot in the aging picture. She said, "There is evidence that older people are trying to maintain their independence as long as possible. The average age at which they enter institutions offering sheltered care is rising."

Lobby for the Aged?

Do the nation's elderly form a persuasive political entity?

Not yet, according to testimony heard recently by a U. S. Senate subcommittee on problems of the aged, but the potential is there. Louis Kuplan, president of the American Gerontological Society, testified that so far the aged are not homogeneous either socially or politically. The witness said he believes, however, that society might turn them into a voting bloc if it continues to treat them as it now does (see Medicine at Work, The Journal, July 27, 1957).

"We could have a gerontocracy instead of a democracy," Kuplan said.

How Teamwork Is Solving . . .

By default, for more than a quarter of a century El Paso General Hospital had been dragging and sagging. Average patient stay was far too long. Extra tax funds, borrowed repeatedly in desperation, barely plugged deficit holes. All three Texas medical schools refused to authorize internship training there. And in the face of a tripling population not a single bed had been added since 1932.

But last month, as a new board of managers took control, plans were blossoming for a new hospital starting next year. It will cost between 4 and 5 million dollars and will be double the size of the present facility by 1962.

There is no magic in El Paso General's turnabout. Rather, the story is one of voter understanding of a critical health problem which was brought to the attention of the community by energetic physicians.

Actually, the El Paso County medical society had not one but two tasks to perform, if it were to give its community the leadership needed to correct a major health deficiency. For many years the hospital had been in trouble. Ostensibly a county facility for indigent patients, it had had to turn to the city of El Paso in recent years for money enough to manage even marginal operation. Even then, the funds appropriated lagged far behind the rising costs and increased patient loads. Everyone agreed the hospital was in bad shape. The question was—what to do about it?

The first action of the El Paso society was to form a fact-finding commission, with community representation, to find out what might be done. After months of study the commission recommended that a hospital district take over operation, maintenance, and expansion.

Since creation of such a district required a

The Hospital of Tomorrow Is Being Planned for Today

No new health facility should be constructed in an area until it has been preceded by a comprehensive survey of the health resources and needs of the area or under the supervision of a competent authority.

Community giving should provide a significant percentage of a patient-care facility's capital needs, to insure a high quality and an appropriate quantity of services.

The nursing home as it relates to the care of our older population overlooks the need of younger people for nursing services.

Such thoughts and recommendations emerged from the workshop sessions of four recent regional conferences devoted to the "development of principles for planning the future hospital system." Sponsored jointly by the Public Health Service and the American Hospital Association the series, ending May 15, brought together physicians and hospital administrators, nurses and educators, architects and insurance officials. All were undismayed by the warning of Dr. Leroy Burney, PHS Surgeon General, that "finding the answers—or, indeed, isolating the relevant questions—will not be easy."

Dr. Burney offered three reasons why the groups should be meeting then to seek planning principles for the hospitals of the future:

—In the hospital insurance business demands for broader coverage without increased premiums have created a dilemma.

—Hospitals can rightly point to forces beyond their control which affect their economy.

—No single element of the nation's hospital system, or those who contribute to its development, can make effective plans on its own; not only are we dependent on one another but we also run a risk of doing real damage to each other and the public by developing isolated plans.

Drs. Robert L. Novy of Detroit and W. C. Stover of Boonville, Ind., both members of the A. M. A. Committee on Medical Facilities, took part in the workshop sessions, which produced statements on such matters as:

PERSONNEL: In planning individual facilities consideration should be given to developing organizational patterns of patient care which will insure the most efficient use of personnel (see Medicine at Work, The Journal, April 26, 1958).

FACILITIES: The general hospital of the future probably will be the focal point of community health emphasis.

CHARITY: Charges to patients, prepayment plans, or health insurance companies should be set at a rate that excludes the cost of care of indigent patients, which is the responsibility of government and private charity.

DUPLICATION: Community planning might avoid unnecessary duplication of expensive or little-used facilities, such as cobalt bombs, radioisotopes, and artificial kidneys.

If the conferees had trouble finding sound infor-

. . . a Texas Health Problem

successful referendum, the medical society's next action was to help form a citizens' committee for the hospital district. In doing so it enlisted the aid of as many local organizations as possible, in an effort to insure widespread support.

The citizens' committee conducted an educational campaign based on two themes—that the hospital district was the most economical way to raise the necessary operating funds, and that all district residents, as well as indigent persons, would automatically be taken to El Paso General if they required emergency treatment.

Every avenue of communication was used to promote the district idea. Background material was prepared for speeches and news stories, telephone committees reached 19,000 property owners, social and civic clubs were taken on tours of the hospital, and speakers were provided for organizational programs.

A major publicity effort was handled by the society's women's auxiliary, who addressed two sets of post card advertisements to a total of 48,000 people.

The effort was a success. Voters last November approved the creation of a taxing district for El Paso General and supplemented it with a thundering eight-to-one approval last April of a $3,700,000 bond issue for new construction. Hospital officials are preparing this month to apply for an estimated $1,500,000 more in Hill-Burton matching funds.

Apparently El Paso County's residents saw the logic of the citizens' committee's often repeated statement that "a well equipped, staffed, and ever ready general hospital is a public insurance policy on behalf of every citizen."

mation on which to base their projections for the future, Dr. Jack C. Haldeman, for one, wasn't surprised. The assistant surgeon general said, "There is probably no other business which spends such a small amount for research. Hospitals spend more than 6 billion dollars a year to bring services to the people and employ more persons than either the auto or steel industries, yet it is estimated they spend less than 5 million dollars annually for hospital research."

What is Dr. Haldeman's estimate of a "reasonable and feasible" amount? Thirty to forty million dollars a year.

Nationwide Hospital Chain?

Inspired by a belief that the independent proprietary hospital may be as old-fashioned as the corner grocery, efforts are under way to establish a nationwide chain of "hospitals for profit." Whether or how this would contribute to hospital planning generally is a question with heavy overtones of economics. According to several published reports the hospital chain will stretch from coast to coast, with sites already being either improved or explored in New York, Illinois, California, and Arizona. All links would lead to Lake Murray Hospitals, Inc., whose president, David Seymour, is quoted as saying, "Accountants tell us that hospitals can be quite profitable in growth areas which now lack facilities and beds."

The Fight to Save VA Intermediary Care

The last shot fired in World War II was also the starting gun in the nation's race to keep its federal medical care programs abreast of a sudden heavy increase in the veteran population. Realizing that former methods of providing this care would be inadequate for the task the Veterans Administration enlisted the aid of the medical profession in setting up a program for outpatient treatment through private physicians. The plan came to be known as "Hometown Care."

On May 1 Hometown Care was the only item on the agenda when representatives of eight state medical associations met in Chicago with Dr. Turner Camp, VA Director of Clinics, and members of the A. M. A. Committee on Federal Medical Services, to discuss the way things were going.

All eight are holders of "Intermediary Contracts" with the VA for outpatient care of veterans with service-connected disabilities. (The Hawaii Medical Association also holds an intermediary contract but could not be represented at the conference.)

The intermediary contract is considered by the Committee to be the most effective of the three plans used by the VA to provide such care. Under this arrangement all contacts between the VA and the physicians are handled by a third party, usually the local Blue Shield plan. The third party negotiates fee schedules, receives and audits all physicians' claims, forwards them to the VA, transmits federal payments to the physicians, and acts as a review agency for both parties.

The nine state associations affected recently received notice that the VA planned to reduce the responsibilities of the intermediaries for fiscal 1960.

After the May meeting Dr. Russell B. Roth, chairman of the Committee, stated in a letter to Mr. Sumner G. Whittier, Administrator of Veterans' Affairs, "Intermediary Contracts, while perhaps not absolutely necessary, are still the best vehicle for bringing together the veteran with service-connected disabilities and the physician in private practice." He also noted that "there is no evidence to show that the VA can handle the functions now performed by the intermediary agencies . . . more economically."

For, lest anyone suspect the profession of a weighty financial interest in these matters, the approximately 38,000 physicians taking part in these VA programs receive an average of $13 per month.

Dr. Russell B. Roth of Erie, Pa., is chairman of the Committee on Federal Medical Services of the A. M. A. Council on Medical Service. Other members are Drs. Vincent W. Archer of Charlottesville, Va., Henry S. Blake of Topeka, Kan., Donald C. Conzett of Dubuque, Iowa, Robert S. Green of Cincinnati, Oscar B. Hunter of Washington, D. C., and J. Lafe Ludwig of Los Angeles. Staff Secretary is Mr. George W. Cooley of Chicago.

¿Habla Español, Doctor?

The call was from the captain of a Finnish freighter berthed at a Milwaukee pier. One of his crew was seriously ill, so he sought medical aid through the Milwaukee Physicians' Service. The request: Find a physician who speaks Finnish.

It wasn't the first such call that had posed a language problem for the medical society of Milwaukee County. Another ship of foreign registry had sought a doctor who spoke Croatian, and an emergency on dry land had pointed up the need to locate a physician with a knowledge of Hungarian.

As a result, the Milwaukee society polled its members and established a list of those with a usable knowledge of a foreign language. "We expect this list to become increasingly important now that the St. Lawrence Seaway is open," a spokesman said.

The benefits to be derived from such a listing are not restricted to port cities, however. The *Bulletin* of the Medical Society of the County of Monroe (Rochester) in New York reports that 65% of its members replied to a similar survey. The poll showed that 102 speak German, 71 speak French, and 58 Italian. Respondents also listed such other languages as Spanish, Polish, Yiddish, Greek, Danish, Lithuanian, and Chinese.

One unexpected dividend of the Rochester survey was the listing of a physician familiar with the sign language of the deaf.

Teeth, Lip Service, and A Schoolside Manner

Q. What is man's most common disease?

A. Tooth decay, which attacks 95% of our population.

Q. How serious are oral disorders?

A. They contribute to many physical, mental, and emotional health problems. Today, 30% of children in any given age group require orthodontic treatment, and it is probable that the present crop of youngsters will lose fully half their teeth by the age of 40.

Those facts, still not fully understood by a substantial segment of the medical profession, are brought out by Harold R. Harlan, D.D.S., of Newark, N. J., to point up the need for improved health programs in schools. Dr. Harlan's point is elaborated by a Doctor of Education, a Doctor of Medicine, and a registered nurse.

"There are barren areas in health instruction, areas which give lip service to it while denying the same in quantity and quality," says Robert E. Schneider, Ed.D., of Waterbury, Conn. "There is need for changed thinking on the part of some who, while condoning the incursion of every imaginable subject, deny a place in the same curriculum for instruction in an area of learning which is as essential to successful living as is instruction in the language which makes learning and communication possible."

A Philadelphia physician, Edward G. Sharp, suggests: "An objective for the school physician is a 'schoolside manner.' This concept assumes the school physician is professionally trained and active in medical and community affairs."

And a registered nurse, Dorothy C. Tipple of Albany, N. Y., noting the changing health needs of children, had this to say. "With the present focus on prevention of juvenile delinquency, we see the school's responsibility to cooperate with parents and with youth agencies in the development of an environment more conducive to social and emotional adjustment."

Those statements represent principles enunciated at the first annual preconvention session on school health, sponsored June 7 in Atlantic City by the 7,000-member American School Health Association in cooperation with the A. M. A.'s Department of Health Education. The 130 physicians, nurses, dentists, and health educators who attended the meeting also heard presentations by Dr. Gunnar Gundersen, immediate past-president of the A. M. A., and Ruth H. Weaver, M.D., immediate past-president of ASHA. By unanimous acclaim the audience recommended that a similar session be held in Miami Beach, prior to the A. M. A.'s next Annual Meeting.

Belief in Lifelong Study Cements the Medical World

Despite differences in language, technique, and tradition the world's physicians find a common ground in the conviction that medical practice carries with it the requirement of lifelong study. This will be evidenced in Chicago beginning late this month when the first of an estimated 1,500 doctors from more than 50 countries is expected to register for the second World Conference on Medical Education. The first was held in London in 1953.

Sponsored by the World Medical Association in cooperation with the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities, the conference to be held Aug. 31 through Sept. 4 will explore all phases of training for the profession of medicine.

The chief aim of the conference, according to Dr. Louis Bauer, secretary-general of the WMA, is to "accelerate the raising of standards of medical education and medical care by providing a world forum for the exchange of opinions on the methods and problems in postgraduate medical training of the physician." To accomplish this aim two of the four conference sections will be devoted to the study of advanced training for physicians, either for specialization or for continuing education. The remaining two sections will deal with basic clinical training and the development of teachers and investigators.

More than 120 speakers from many parts of the world have been invited to address either the plenary sessions or one of the section groups. Language differences will be accommodated by a simultaneous translation of all proceedings into English, French, and Spanish.

Such an international conference has been termed "invaluable" by Dr. Victor Johnson, deputy president of the conference and director of the Mayo Foundation for Medical Education and Research. He said, "It will be a medium for the exchange of ideas and discoveries, a stimulus to greater efforts directed to a better understanding of man and nature, and a means of fostering good will and friendship between the peoples of the world."

That this is more than just a pious hope is indicated by the fact that the Soviet Union, although not a member of WMA, is expected to send a delegation to the conference and will have two speakers on the program. Poland, another nonmember, will also be represented.

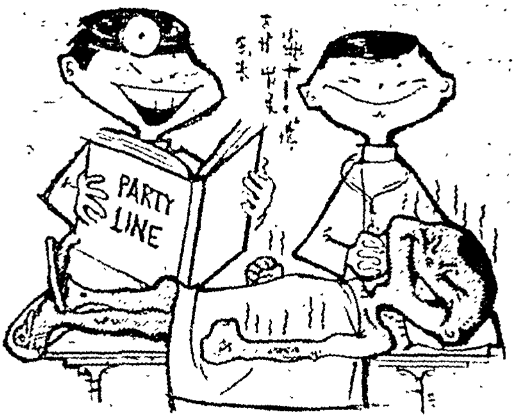
Party Line to the Rescue In Red China Medical Tale

If your medical miracles haven't been up to par lately, maybe you are politically disoriented. . . .

That point is made in a recent *Chinese Medical Journal* editorial which tries patiently to explain how extraordinary medical results can be achieved "when politics take the lead over scientific theory."

It seems that politically shortsighted Chinese physicians "unanimously predicted an unfavorable prognosis" when a steelworker suffering burns over "89.3% of the body surface" was brought to a Shanghai hospital. But, the editorial continues, no sooner had the assembled physicians shaken their heads in fatalistic despair than "a message was received from the Party Committee at the Shanghai Third Steel Mill pleading—for the sake of steel production and in order not to disappoint the workers of the whole mill—to save the wounded worker at all cost." This got the ball rolling, it appears, and the medical school's Party Committee quickly "analyzed the ideologic state of the doctors, and correctly pointed out that what could not be done in capitalist countries we could do."

A "case history" accompanying the straight-faced editorial is sparse in clinical detail but rife with melodrama and ideological therapeutics. Once their "initial error" had been made plain to them, the physicians were reported to have learned rapidly. "It's true that diseases can be treated by Marxism-Leninism," they allegedly chorused. "We shall make it our duty to cure all patients henceforth with burns within 90%."



By this time the general enthusiasm seems to have infected even the patient, who is quoted by the so-called medical journal as saying, "Cure me; I'm needed in production. I can leave my wife and child, but not my furnaces." Turning to his wife, who had brought his pay, he demanded to know, "Have you paid my Party dues?"

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THE DIABETIC AND HIS EMPLOYMENT

GUEST EDITORIAL

Jean S. Felton, M.D.

MECHANIZATION and automation in today's industries have made possible the greatest potential utilization in history of workers with some degree of disablement. This change in production methodology has not necessarily resulted in the employment of all physically marginal persons, but has altered the physiological demands of jobs so that those with some capacity could work.

Outstanding in his effective contribution to the fabrication of the world's goods has been the diabetic, whose work situation has been aided even more by the introduction and use of orally given hypoglycemic agents. Recognizing this addition, the Committee on Employment of the American Diabetes Association has recently reissued its Statement on Employment of Diabetics,[1] originally offered in 1952, and revised at intervals. Criteria are offered as guides in their employment in industry or business.

To the prospective employer and the interested physician examining applicants for work, diabetics fall into several groups. The mild diabetic, whose condition is diet-controlled, in no need of insulin, and the selected diabetic, whose condition is controlled by a sulfonylurea compound and diet, present no problem in employment. Of a third group, severe diabetics, requiring both insulin and diet regulation, the well-controlled, well-regulated, cooperative patient should be accepted for work. It is the comparably categorized diabetic, however, who becomes the poor employment risk because of lack of control and regulation. Not only is this unstable clinical state a difficult one to care for in competitive industry and commerce but it is fraught with the constant threats of complications and absenteeism. Unnecessary prejudice against all diabetics can result from the injudicious employment of the patient who is not motivated to good self-care under medical counsel.

In a survey conducted by the Committee on Employment of the A. D. A.,[2] it was learned from 127 companies with a total of 1,900,000 workers that 69% employed known diabetics. Regarding their "experience as to reliability and absenteeism," 51% felt it to be satisfactory and 47% claimed it to be "same as average worker." There were differentials in hiring among the varieties of industries questioned, with five out of five railroads, as an example, indicating that they do not employ persons with diabetes. The percentage of diabetics in the companies reporting was 0.58%, a little under the average for diabetics in the general population, estimated at 0.75%.

The Committee on Employment has offered these suggested standards for employment: 1. The diabetic job applicant should bring a statement from his physician stating that he is controlled and is examined periodically. 2. Although the diabetic can perform any work for which he has physical, mental, and educational capacities, those who take large doses of insulin should not be assigned work wherein hypoglycemic attacks might lead to injury to themselves or others. In those under control solely by an oral preparation, symptomatic hypoglycemia is not a factor. 3. The diabetic should work the same hours in a steady shift, but if he must rotate he should avoid the midnight to 8 a. m. tour. 4. It is wise to have key people in labor and management informed of the nature of diabetes and the possibility of coma or insulin reaction, and the decision regarding this should be left with the plant physician. 5. The diabetic should carry a card with him which identifies his condition. 6. When the usual laboratory facilities on the outside are available only during working hours, time for the company can be saved and the employee helped by having the industrial medical department perform frequent blood sugar and urine examinations. 7. An annual physical examination should be made on each diabetic. 8. The plant physician is within his rights if he requests another work assignment for the diabetic, when new complications create additional risks. 9. The insulin-requiring diabetic should be considered controlled if the fasting blood sugar level is not below normal and not above 150 mg. per 100 cc. of blood, the three-hour postprandial level is not higher than 250 mg. per 100 cc., all by the Folin-Wu method, and he is under regular medical supervision.

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[1] Employment of Diabetics, Statement of the Committee on Employment, American Diabetes Association, from the Report of the Committee, as accepted by the Council of the Association, June 7, 1952, New York, American-Diabetes Association, June, 1958.

[2] Analysis of Survey Concerning Employment of Diabetics in Some Major Industries, Organization Section, Diabetes 6:550 (Nov.-Dec.) 1957.

These standards, or criteria, are practical ones, and the time concession is the only one asked for the well-controlled diabetic worker. Persons with this condition have worked well in nearly all types of employment, and their production, attendance, and low injury records bespeak the wisdom of the utilization of this manpower. The blocks to their acceptance, as with other somewhat physically limiting conditions, are to be found in false, prejudicial, frequently rationalized thinking, based on unsound emotional responses of the prospective employer.

It is through the enlightened help of the physician and the employer that more diabetics will be given opportunities to demonstrate their skill on the job. Needing little medical surveillance while at work, they can make a considerable contribution to the production of the world's goods.

THE NEW CUMULATED INDEX MEDICUS

An agreement has been made with the National Library of Medicine in Washington, D. C., whereby the American Medical Association will publish annually in cumulated form the bibliographic references which appeared in the preceding year in the Index Medicus, a name which the present Current List of Medical Literature will assume in January, 1960.

The offer of the National Library of Medicine to provide the American Medical Association with the cumulated copy in film form was accepted by the Board of Trustees at the Atlantic City meeting in June, at which time the trustees decided also to discontinue publication of the Quarterly Cumulative Index Medicus with volume 60 (July-December, 1956), which volume recently was mailed to its subscribers. The format of the new Cumulated Index Medicus will be closely like that of the Quarterly Cumulative Index Medicus, and it will eventually provide a truly world-wide coverage of medical literature, probably as many as 180,000 titles.

The American Medical Association will publish independently of the government and at its own cost the new Cumulated Index Medicus, and the Superintendent of Documents at the Government Printing Office in Washington, D. C., will continue to sell the monthly index published for many years by the National Library of Medicine. Those hospitals, libraries, and individuals who have been subscribers to Q. C. I. M. and who desire to fill the gap—1957-1958-1959—will be able to obtain copies of the Current List of Medical Literature for those years, through the National Library of Medicine.

The ever-increasing amount of medical literature and the difficulty since World War II of finding personnel fitted for this specialized work caused the Q. C. I. M. to fall behind its former schedule almost two and one-half years. The same conditions caused the National Library of Medicine to survey the field for additional help and finally to adopt modern machine methods which will do rapidly what heretofore has been done by hand.

While this change-over has affected some 27 faithful and devoted employees who worked on the Q. C. I. M., most of them have either been agreeably assigned to other positions in A. M. A. headquarters or have been able to obtain positions elsewhere. The devotion of these employees to Q. C. I. M., an index which was long a favorite of physicians and other medical investigators throughout the world, is gratefully acknowledged.

Dr. John Shaw Billings and Dr. Robert Fletcher started the first Index Medicus in 1879 at the Army Medical Library. The American Medical Association began publishing the Quarterly Cumulative Index to Current Medical Literature in 1916. The two indexes were combined in 1926 and published by the American Medical Association as the Quarterly Cumulative Index Medicus with the financial assistance of the Carnegie Institution in Washington, which contributed toward the expense $10,000 per year for five years. The Quarterly Cumulative Index Medicus has never been a self-sustaining venture, and since the termination of the agreement with the Carnegie Institution it has cost the Association many thousands of dollars a year. Nevertheless, the trustees looked upon this project as one of the finest of many efforts that the Association has made to aid world progress in medicine. Now that the Q. C. I. M. has been discontinued, another—the annual Cumulated Index Medicus—will take its place.

A. M. A. DISAVOWS VITAMIN ADVERTISEMENT

An advertisement which cleverly implies endorsement by the American Medical Association of a brand of vitamin capsules has been strongly disavowed by the A. M. A. The book entitled "Book of Health," edited by an A. M. A. employee, was offered free by Vitasafe Corporation, New York City, along with a supply of their capsules. The words, "The Official American Medical Association Book of Health" show up prominently in the advertisements appearing in newspapers and magazines along with a photograph of a bottle of the capsules. This was done without A. M. A. knowledge or approval.

The A. M. A.'s official statement regarding vitamins (THE JOURNAL, January 3, 1959, page 109) states that, if a healthy person's diet contains the key food groups in sufficient amounts, nutritional supplementation is unnecessary. There has been no change in this policy.

COUNCIL ON NATIONAL DEFENSE

The following paper is being presented through the Council and its Committee on Disaster Medical Care as a matter of interest to physicians and hospitals interested and active in medical civil defense preparedness.

FRANK W. BARTON, *Secretary.*

FUNCTIONS OF A HOSPITAL IN A MAJOR DISASTER

Frank F. Schade, M.D., Los Angeles

It is the accepted obligation of our profession to give the very best possible medical care to our fellow citizens at all times and under any circumstances. This, of course, includes disaster medical care.

Disasters can strike any time, any place, and they need not be caused by war to be of major proportions. What is a major disaster? It must be relative, depending on the locality affected. As an example, a fire or earthquake that would destroy a dozen blocks in a smaller city could be considered major, but it probably would not be so thought of in one of our larger cities.

To oversimplify the answer, the functions of a hospital are to furnish the best possible medical care to the victims of a disaster, under the existing conditions. There are three principal possibilities of hospital involvement and function.

Disaster in Hospital Itself

The first possibility is in the event the hospital itself is involved in a disaster; this could be limited to any one hospital, as in the event of a fire or explosion in the hospital. In this situation, as in all of the others, the basic premise is that carefully considered plans have been drawn up and then tested and retested until they are so modified that they are as nearly perfect as humanly possible. The very first consideration of any hospital should be for this contingency and is concerned with rapid evacuation of patients and personnel. This may sound simple, but actually it involves a myriad of details. For every method or action, there must be a substitute in the event something would prevent its accomplishment. If a certain door is planned for an exit, there must be an alternative choice in case the door be blocked by flames or a fallen beam or simply jammed. If there are elevators, what is to be done if power fails?

If there is not time to remove all patients, which will you evacuate and which will you—yes—abandon? This type of decision is most difficult to make under the best of planning conditions but is impossible to make under the stress of the emergency. A priority system is one of the essentials and should be based on the future value of that person to the community. It follows that the highest priority should be given to children without preexisting handicaps, to women in the childbearing age, and to other younger adults. The aged, those suffering from incurable conditions and advanced degenerative disease, should have the lowest priority. This is a repugnant thought but it is a decision that possibly could be forced on us. It exemplifies one of the basic tenets of all disaster work, no matter what the branch—do the best for the most.

Planning must include a place that can be used as a substitute for the hospital, to which the evacuated patients can be taken. It should not be too near the hospital, otherwise it could also be involved in the incident that caused the hospital to be abandoned. Transportation must be considered, and large flat bed trucks, such as moving vans, are ideal for the mass movement of patients.

If time and available personnel permit, small, essential supplies and equipment should be removed from the hospital, perhaps in pillow cases. Antibiotics, sedatives, antiseptics, analgesics, dressings, small instruments, syringes, and needles are but a partial list of things more urgently needed. A definite understanding, preferably in writing, to cover this emergency removal should be had with the hospital ownership and/or management. A rendezvous point for the staff, personnel, and employees of the hospital should be known to all concerned. This could well be the place of the substitute or auxiliary hospital.

Disaster in Hospital and Area

The second consideration is of the hospital that is located in a disaster area not limited to the hospital itself. It divides itself naturally into two possibilities —with and without warning of the disaster. Warning is possible, both in war and natural disasters. If there is no warning, then the previously discussed considerations would apply.

Chief, Medical and Health Section, Los Angeles County and Cities Civil Defense Planning Board.

If there is warning, complete, orderly, and less hurried evacuation and dispersal can be accomplished. Larger and more complete lists of the smaller items of supply and equipment can be removed, including canned and packaged food supplies and some cooking equipment. A new word and concept, "dispersal," enters here—this, in contradistinction to the previously considered evacuation. One of the objectives in dispersal is the actual discharge of the maximum number of convalescent patients, either to the family or to a welfare service. There are a number of reasons for this.

A much greater degree of cooperation also becomes necessary—cooperation, undoubtedly with other hospitals and certainly with other services of the disaster organization. Communications, transportation, supply, welfare, and traffic control are those services that would be involved in this phase.

During dispersal it is probable that the patients from several hospitals would be consolidated into one convoy to go to a common destination. Attendants must accompany these patients and certainly should include any house staff, nurses, and aides. It would also be most desirable for some of the attending staff to go along. These dispersees will be patients, some quite ill. The trip could take many hours, so some of these patients could require considerable attention en route.

Hospitals in Support Areas

All of the hospitals in the disaster areas must have plans for the reception and care of disaster victims. This phase can be discussed in the third and final category of hospitals that are located in the reception or support areas.

The cardinal functions of hospitals in the support areas are (1) the discharge of the maximum number of convalescent patients, (2) implementation of expansion plans, (3) reception of and care of dispersed patients and disaster casualties, and (4) assistance in setting up and operating emergency hospitals. In view of the first two functions, for the satisfaction of all concerned, reliable and accurate intelligence is a requisite. It is very easy to visualize the utter demoralization that would result in any support area if the word were passed to put these plans into operation and then to have them later rescinded.

Obviously the first step in making room for an anticipated or actual flood of patients is to discharge every possible patient currently in the hospital, to family, friends, or the welfare service. If there should be any urgency in this, as there could well be, it is essential that two provisions are agreed on in advance by the staff. The first is a current grading system of all hospital patients, designating those who can be immediately discharged, those for whom some degree of medical supervision is desirable, and those who should be evacuated or dispersed and remain in the system of medical care. The second is the delegation of the necessary authority, based on the grading system, to certain persons to go through the hospital and actually order the discharges of the patients, without the actual consent at the moment of the patients' attending physicians.

The next step is the implementation of the expansion plan. Every available square foot of space must be used. This does not mean simply converting private rooms to capacity of two or three patients. Auditorium, class rooms, solariums, halls, and any other available space must be used. If there is a nurses' residence and/or a separate building for a school of nursing, this would be very important for convalescent patients and possibly for the obstetrical department.

In the plan, careful attention should be given to admission of patients; this may require that the admitting department be relocated. In many hospitals this department could not possibly take care of mass admissions. Available entrances, streets, driveways, and parking lots are factors to be considered, as well as adequate space. Planning should also provide for a first-aid facility forward of the admitting area to screen out the lesser injured and thus reserve hospital space and care for only the most acute and serious cases.

Either adjacent to or very near the admitting area should be a large area for triage and resuscitation. This is one of the most important departments and should be supervised by one of the best and most experienced surgeons, who is mentally and emotionally well adjusted and stable. This requirement cannot be overemphasized, for he will have to make the decisions as to which patients will be cared for first, which ones can wait for hours, and even which ones must simply be kept as comfortable as possible until they die. The basic principle is to use all facilities most efficiently, and this means that the highest priority for surgical care will be for those patients requiring short—and the word short demands emphasis—lifesaving procedures. In a major situation an operating room cannot be retained for three or four hours for one patient when several others could be cared for in the same period of time.

The expansion plan includes the provision of additional surgical facilities. This may be accomplished in several ways; some large operating rooms can have two tables instead of one, additional operating rooms frequently can be created in the surgical suite, and consideration should be given to the use of delivery rooms for surgery. More efficiency of operation is frequently achieved if certain floors or areas of the hospital are designated for particular types of cases, as for burns, fractures, and postoperative care.

Kitchens can rarely be enlarged, but attention should be given to altered schedules and types of food. Most of the acutely ill patients will get liquids. The biggest problem will be that of feeding all of the personnel who will remain at the hospital for a number of days on around-the-clock schedules.

Laboratory work will be very limited in its scope. Large quantities of blood will be necessary, so blood procurement must be arranged for. This area must be readily available to donors and should be located so that this traffic does not interfere with patient and attendants traffic flow. In many hospitals this will require that it be set up away from the existing laboratory.

Finally, provision must be made for adequate morgue space, since this type of disaster results in an unusually high mortality rate.

Provision should also be made for an auxiliary to the hospital, with minimal equipment, to which convalescent patients can be transferred as soon as their condition warrants it. This is necessary to keep bed space available for the constant flow of acutely ill patients admitted, that could very well extend over a number of days.

Another function that poses a perplexing personnel problem is concerned with the 200-bed emergency hospitals. Our plan is to use these units as nuclei around which will be created hospitals of from 500-bed to 1,000-bed capacity. Many of the units have been prepositioned in localities considered to be safe distances from anticipated danger zones. These safe areas naturally are in the more sparsely populated counties. The problem is compounded by the expected tremendous increase in the population of these counties, of both well evacuees and those requiring medical care and treatment of wounds, plus the normally small number of medical and allied personnel and the few hospital beds available in these counties. The only possible answer is the reinforcement of the expanded existing hospitals by these enlarged emergency hospital units.

In a situation of dispersal, these units should be set up at their original capacity and be used to care for the hospital patients from the danger zones. This would permit the personnel to become familiar with the hospital under the most favorable conditions and at the same time would conserve the beds in the existing hospitals for the first influx of casualties. On notification of the occurrence of the disaster, expansion could be affected. If the disaster occurred without warning, the units would be set up at once at their expanded capacity.

The personnel shortage will eventually be greatly alleviated by the arrival of medical and allied personnel from the dispersed areas. A few will arrive with the convoys of the hospital patients. Others will come to the area by prearrangement or as members of the dispersed population. Suddenly, under the most unfavorable professional and emotional conditions, there will be thrown together doctors from different sections of the state who have widely differing backgrounds of culture, training, ability, and experience. Here is where cooperation, understanding, teamwork, and the suppression of professional pride and vanity will be important.

As the dispersed persons arrive, an additional function of the hospitals, and especially the improvised emergency type, will be to furnish care for these people. Hospitalization by necessity must be restricted to the care of only the patients with the most acute and urgent conditions. Many patients who normally would be treated in hospitals will be cared for in some other manner. This same type of minimal care will also apply to the resident population.

A few of the basic concepts relative to the functions of hospitals in major disasters have been superficially discussed. Briefly stated, the functions are (1) the protection and safeguarding of the present hospital patients, (2) the best possible care of the disaster victims, under the circumstances, following the dictum of doing what is best for the most, (3) minimal care for the resident population, and (4) minimal care for the dispersed.

GOVERNMENT SERVICES

AIR FORCE

Space Medicine Course.—The School of Aviation Medicine will offer a new advanced course in aerospace medicine to senior medical officers from the air forces of our allies at its new home at Brooks Air Force Base, Texas. The starting date for the first course is Sept. 8. Prerequisites for attendance in the 27-week course include prior satisfactory completion of the primary course in aviation medicine conducted by the school; a minimum of one year of practice in aviation medicine subsequent to completion of the primary course; and a reading, writing, and speaking knowledge of the English language. The purpose of the course is to prepare allied senior medical officers for professional responsibilities as aviation medicine consultants, investigators, teachers, and directors of programs in their respective air forces. The course will consist of 1,078 instruction hours, divided into three parts: part 1, academic aviation medicine; part 2, physiological training program; and part 3, practical aspects of aviation medicine. The latter will be conducted at air training command bases with instruction and supervision by practicing air force flight surgeons.

Personal.—Col. Lawrence J. Milch, chief of the department of pharmacology-biochemistry at the Air Force School of Aviation Medicine and recent winner of the Air Force's commendation medal for his work in heart diseases and motion sickness, will become deputy commander of the 6,102nd Air Base Wing at Yokota, Japan.

ARMY

Personal.—Brig. Gen. Thomas J. Hartford, Army Medical Corps, was appointed deputy surgeon general of the United States Army. His predecessor, Major Gen. James P. Cooney, has been named chief surgeon, U. S. Army, Europe.

PUBLIC HEALTH SERVICE

Dr. Freund Honored.—Dr. Jules Freund, internationally known immunologist, was selected as recipient of a special citation from the Allergy Foundation of America. Dr. Freund is in charge of basic studies on allergy and immunology at the National Institutes of Health, U. S. Public Health Service, Bethesda, Md. The allergy foundation is a nonprofit organization which operates a program of public and professional education and training in the field of allergic diseases with headquarters at 801 Second Ave., New York 17. One of Dr. Freund's most important contributions was his demonstration of the increased effectiveness of vaccines in which the protective materials are incorporated in water-in-oil emulsions. The latter, known as Freund's adjuvant, has provided tools used routinely in basic laboratory research by immunologists here and abroad.

New Indian Service Hospital.—The Public Health Service awarded a $1,391,700 contract for construction of a 50-bed hospital and staff living quarters at Sells, Ariz., to serve the Papago Indians. Since 1947, when the Oasis Hospital at Sells was destroyed by fire, Papago Indians have been served by the Public Health Service Indian Hospital at Tucson, 150 miles away. The new hospital will include outpatient and field health facilities for additional services to about 8,000 beneficiaries living in 73 isolated villages of the 4,000-square mile Papago Reservation. The new, centrally-located hospital should be completed by 1961.

NATIONAL SCIENCE FOUNDATION

Postdoctoral Awards.—Applications will be accepted through Sept. 1 by the National Science Foundation for a second group of postdoctoral fellowships. Fellowships will be awarded in medical and other science fields. Names of successful fellowship candidates will be announced on Oct. 15. To be eligible for postdoctoral fellowships, candidates must be citizens of the United States with special aptitude for advanced training and must hold the doctoral degree or have the equivalent in training or experience. Fellows will be selected on the basis of ability as evidenced by letters of recommendation and other evidence of scientific attainment. Candidates' qualifications will be evaluated by carefully chosen panels of scientists operating under the aegis of the National Academy of Sciences–National Research Council. Final selection on fellows will be made by the National Science Foundation.

A stipend of $4,500 per year will be awarded to successful applicants. Dependency allowances will be made to married fellows. Fellows may engage in study and/or research at any accredited nonprofit institution of higher education in the United States or any nonprofit foreign institution of higher education. A limited allowance to aid in defraying a fellow's cost of travel will also be available. Application materials may be obtained by writing to the Fellowship Office, National Academy of Sciences–National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C.

Research Laboratories.—The National Science Foundation has a new program for renovation and/or construction of graduate level (doctoral) research laboratories at institutions of higher education. Generally speaking, equipment to be supported will be limited to standard fixed equipment (e. g., laboratory benches, built-in refrigerators, etc.), whether the grant is for construction of a new laboratory or the renovation of an existing one. Proposals pertaining to laboratories for research use in any area of the basic sciences will be considered, but the foundation will not consider requests for support of facilities to be used primarily for instructional purposes. Grants made under this program will require matching by the institution, from nonfederal sources, to the extent of at least 50% of the direct costs to be incurred. Proposals should be submitted to the division of biological and medical sciences, National Science Foundation, Washington 25, D. C., by Dec. 1, 1959. In most cases it will be helpful to address an inquiry to the appropriate division of the foundation before preparing the proposal. It is anticipated that grants under this program will be made about June 1, 1960.

MEDICAL NEWS

COLORADO

Dr. Stonington Named Division Head.—Dr. Oliver G. Stonington, member of the volunteer faculty of the University of Colorado School of Medicine, Denver, since 1950, was named head of the division of urology in the department of surgery on a full-time basis. The appointment is effective Sept. 1. The position previously has been filled by volunteer faculty members on a part-time basis. Dr. Stonington is a diplomate of the American Board of Urology. He reportedly was instrumental together with Dr. Joseph H. Holmes, professor of medicine, in introducing the artificial kidney to the University Medical Center with which more than 250 patients have been treated.

GEORGIA

State Medical Election.—Officers for 1959-1960 of the Medical Association of Georgia are: president, Dr. Luther H. Wolff, Columbus; president-elect, Dr. Milford B. Hatcher, Macon; immediate past-president, Dr. Lee Howard Sr., Savannah; first vice-president, Dr. Corbett H. Thigpen, Augusta; second vice-president, Dr. Walter P. Rhyne, Albany; secretary, Dr. Christopher J. McLoughlin, Atlanta; speaker of the house, Dr. Thomas W. Goodwin, Augusta; vice-speaker of the house, Dr. Fred H. Simonton, Chickamauga.

HAWAII

Health Record of New State.—Statisticians of the Metropolitan Life Insurance Company reported that tuberculosis mortality in the civilian population of Hawaii was down to 3.1 per 100,000 in 1957, a decrease of more than 50% in two years and of about 95% since 1940. The 1957 death rate from influenza and pneumonia was only 25.6 per 100,000—half that of 1940. At the same time, the principal communicable diseases of childhood (measles, scarlet fever, whooping cough, and diphtheria) and typhoid fever have been practically eliminated as causes of death. The infant mortality rate in 1957 was 24 per 1,000 live births, compared with 44 in 1940. Currently three-fourths of the infant deaths occur in the first month; the comparable proportion in 1940 was three-fifths. Over the same period, maternal mortality has dropped from 2.4 per 1,000 live births to 0.4. Leading causes of death in Hawaii are heart disease (first) and cancer (second). Next in order were diseases of early infancy, cerebral hemorrhage, accidents, and influenza and pneumonia. Accidents are the leading cause of death in the 1-24 age group, nearly 45% of the fatal accidents in this age group resulting from motor vehicle mishaps. Longevity in Hawaii compares with that for continental United States. According to the life table for 1949-1951, the latest available for Hawaii, the average length of life for males was 67.76 years. The average for females was 71.29 years.

ILLINOIS

Society News.—Dr. Charles K. Petter, Waukegan, was reelected president of the Illinois Tuberculosis Association May 25 at the annual meeting in Chicago. Reelected treasurer of the organization was Dr. Jesse A. Stocker, Springfield. Meeting in conjunction with the association was the Illinois Trudeau Society, medical section of the state tuberculosis association. Officers elected were: president, Dr. Darrell H. Trumpe, Springfield; president-elect, Dr. Meyer R. Lichtenstein, Chicago; and secretary-treasurer, Dr. Raymond H. Runde, Peoria.——The officers for the Illinois Society of Pathologists for the coming year are Drs. Franklin J. Moore, Chicago, president, and James R. Thompson, Chicago, secretary-treasurer. The president of the society is the chairman of the pathology section of the Illinois State Medical Society and the secretary-treasurer is the secretary of the section.

KENTUCKY

Personal.—Dr. George W. Pedigo Jr., Louisville, recently became the first physician ever to be appointed to the Board of Directors of the Kentucky Chamber of Commerce. Dr. Pedigo is associate editor of the *Journal of the Kentucky State Medical Association*, vice-speaker of the house, and was recently elected president-elect of the Jefferson County Medical Society.——Dr. Daryl P. Harvey, Glasgow, was appointed by President Eisenhower as a member of the President's Citizens Advisory Committee on the Fitness of American Youth. This committee, which serves in an advisory capacity to the Council on Youth Fitness, considers and evaluates "existing and prospective governmental and private measures conducive to the achievement of a happier, healthier, and more completely fit American Youth." Membership is appointed from all sections of the nation. Last November Dr. Harvey was appointed a vice-chairman of the 1960 White House Conference on Children and Youth. Dr. Harvey is currently serving as president of the Kentucky Academy of General Practice.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

MASSACHUSETTS

Professors Retire.—Three professors retired from Harvard University on July 1, to become professors emeriti. They are Dr. Leland S. McKittrick, Brookline, clinical professor of surgery; Dr. Joe Vincent Meigs, Boston, clinical professor of gynecology; and Dr. Francis C. Newton, Boston, clinical professor of surgery. Dr. McKittrick has been associated with Harvard Medical School since 1932. Dr. Meigs has served as clinical professor of gynecology at Harvard since 1941 and has been associated with the Medical School since 1932. Dr. Newton was appointed in the department of surgery at Harvard as an associate in surgery in 1920.

Personal.—Dr. Walter F. Lever, of Chestnut Hill, who was associated with Harvard Medical School and Massachusetts General Hospital, will be the principal investigator of a new research department in dermatology at the Boston Dispensary. He will head the department of dermatology and syphilology at the dispensary. He also has been appointed clinical professor of dermatology at Tufts College Medical School.——Dr. Robert R. Mezer, of Boston, was appointed coordinator of the psychiatry training program at the Boston University Law-Medicine Research Institute. Dr. Mezer will also serve as assistant professor of legal psychiatry at the university's School of Law, and an assistant professor of psychiatry at the university's School of Medicine.——Dr. Robert H. Hamlin, Washington, D. C., assistant to Arthur Flemming, Secretary of the Department of Health, Education and Welfare, resigned to become professor of public health administration in the Faculty of Public Health at Harvard University, Boston.

Program in Pharmacology and Biostatistics.—A training program in clinical pharmacology and biostatistics related to diseases of the heart and blood vessels was established at the Lemuel Shattuck Hospital in Boston and the Harvard Medical School under a grant from the National Heart Institute of the National Institutes of Health. The program, which opened July 1, includes a combination of on-the-job training in the planning and execution of therapeutic trials and formal instruction in research techniques related to clinical pharmacology. Both the pre- and postdoctoral candidates will participate in the program. Course work will be available at the Lemuel Shattuck Hospital, the Harvard Medical School, and the Harvard School of Public Health. The candidates will be concerned with research projects in progress at the hospital. Dr. Frank A. Howard, research associate in pharmacology at Harvard, will direct the program in collaboration with Dr. Mindel C. Sheps, Boston, assistant professor of preventive medicine, and Dr. Thomas C. Chalmers Jr., Boston, clinical associate in medicine at Harvard. Candidates for the postdoctoral degrees are required to have an M.D. degree and should have completed the first portion of their training in internal medicine. Predoctoral candidates must have a B.A., M.S., B.S., or Ph.D. degree. Medical students will be required to have the recommendation of the dean of the faculty of medicine in their universities.

MICHIGAN

Dr. Hubbard Named Dean.—Dr. William N. Hubbard Jr., associate dean of the New York University College of Medicine, New York City, was appointed dean of the University of Michigan Medical School, Ann Arbor. The new dean succeeds Dr. Albert C. Furstenberg, who has headed the Medical School since 1935. Dr. Hubbard is the fifth person to carry the title of "dean" and the eighth to serve as administrative head of the Medical School since it was founded in 1850.

Dr. Foust Goes to Africa.—Dr. Joseph C. Foust, general practitioner from Ionia, left June 19 to spend a lifetime in the back country of Tanganyika, sponsored by the Foundation for All Africa, Inc., a nonsectarian group that devotes itself to furthering "person-to-person" contacts between Africans and Americans. Dr. Foust is taking along a truck, a house trailer, and his wife and six children. He is paying for the trip himself and "will devote his time to treating sick natives." "The decision to go to Africa was taken about a year ago," Dr. Foust said. "It is a matter of charity and justice." The family disembarked at Capetown in July to start a 1,500-mile drive to the village of Mboya on the south-central plains of Tanganyika.

MINNESOTA

Personal.—Dr. Walter A. Fansler, emeritus clinical professor of surgery, University of Minnesota Medical School, Minneapolis, was made an honorary member of the Royal Society of Medicine (Proctologic Section) at the joint meeting of the Royal Society of Medicine and the American Proctologic Society in London, England, July 1.——Dr. R. Drew Miller, consultant in medicine in the Mayo Clinic and assistant professor of medicine in the Mayo Foundation, Graduate School, University of Minnesota, was appointed assistant director of the Mayo Foundation by the board of regents of the University. Dr. Miller will continue to devote about half his time to the practice of internal medicine in the Mayo Clinic.——Dr. Reginald G. Bickford, head of the electroencephalographic laboratories of the Mayo Clinic, Rochester, was appointed a member of the Neurology Study Section of the National Institutes of Public Health, a unit of the U. S. Department of Health, Education and Welfare.

Personal.—Dr. Edward J. Van Liere, Morgantown, dean of the West Virginia University School of Medicine, has been elected an affiliate of the Royal Society of Medicine, London, England. The society was founded in 1805 and chartered in 1834.—— Dr. Robert P. Hagerman, recently retired from service with the Department of Justice, has been named by Dr. Richard J. Lilly, head of the West Virginia State Department of Mental Health, as superintendent of Weston State Hospital. He succeeds Dr. Lilly, who has served as superintendent during the past several months.

WYOMING

State Medical Election.—Elected officers of the Wyoming State Medical Society are: Drs. Benjamin Gitlitz, Thermopolis, president; Francis A. Barrett, Cheyenne, president-elect; S. J. Giovale, Cheyenne, vice-president; Frederick H. Haigler, Casper, secretary; Carleton D. Anton, Sheridan, treasurer; Albert T. Sudman, Green River, delegate to A. M. A.; and Bernard J. Sullivan, Laramie, alternate delegate to A. M. A.

GENERAL

Change of Address.—Mail intended for the Joint Commission on Mental Illness and Health, its officers, or its staff should be addressed as follows: Joint Commission on Mental Illness and Health, Massachusetts Mental Health Center, 74 Fenwood Road, Boston 15. Following conclusion of the study projects of the National Mental Health Survey on June 30, editorial offices will be maintained at the new address until publication work on the monograph series and final report is complete.

Books for Philippine Medical Library.—A request for medical books and journals from A. M. A. members has been received from Dr. Mercedes V. Planas, of Cebu City, Philippines, for the Cebu Medical Library. The organization, "Books for Asian Students," has agreed to handle the shipping. Publications should be shipped by motor freight, collect (not Railway Express or moving van). The shipment should be addressed to Cebu Medical Library, % Books for Asian Students, 21 Drumm St., San Francisco 11, Calif. Packing in ordinary cardboard cartons tied with rope is sufficient. Packages will be repacked for overseas shipment. Dr. Planas' address is P. O. Box 55, Cebu City, Philippines.

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as [illegible] **to Tour Russia.**—Six American physicians
[illegible]change mission to Russia on Sept. 5,
NEW [illegible]land. They are Drs. Cl[illegible]
New Yor[illegible] William B. C[illegible]
Break Grou
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tutes and laboratories and then start a month-long itinerary which will include Leningrad, Sochi, Sukhumi, Kiev, and Odessa. Dr. Barborka, president, American Gastroenterology Association, is taking a previous tour to coordinate a program of medical researches in gastroenterology, which will take him to Sweden, France, Spain, the Netherlands, Germany, England, and Switzerland.

Otorhinolaryngological Congress in Paris.—The 57th French Congress of Otorhinolaryngology will take place Oct. 19-22 in the Grand Amphitheater of the Faculty of Medicine, rue de l'Ecole de Médecine, under the presidency of Dr. Andre Soulas, of Paris, and the honorary presidency of Prof. L. Binet, dean of the Faculty of Medicine of Paris. The program includes presentation of papers, and two reports will be discussed: (1) Surgery for Deafness—Its Present State, Its Future, and (2) The Laryngologist and Actual Data on Treatment of Acute Respiratory Insufficiencies. An exposition of surgical instruments, appliances, and pharmaceutical specialties will be held in the Hall of the Faculty. For information, write the General Secretary, Dr. Henry Guillon, 6, Avenue MacMahon, Paris 17, France.

Research Fellowships and Grants.—The Life Insurance Medical Research Fund is receiving applications for two types of awards to be available July 1, 1960, as follows: (1) Until Oct. 15, 1959, for postdoctoral research fellowships. Candidates may apply for support in any field of the medical sciences. Preference is given to those who wish to work on fundamental problems, especially those related to cardiovascular function or disease. Minimum stipend is $4,500 with allowances for dependents and necessary travel. (2) Until Nov. 1, 1959, for grants to institutions in aid of research on cardiovascular problems. Support is available for physiological, biochemical, and other basic work broadly related to cardiovascular problems as well as for clinical research in this field. Information and application forms may be obtained from the Scientific Director, Life Insurance Medical Research Fund, 345 E. 46th St., New York 17.

Occupational Health Congress in New York.—The 13th International Congress on Occupational Health will be held July 25-29, 1960, at the Hotel Waldorf-Astoria, New York City, organized under the auspices of the International Association on Occupational Health. The program will include physicians, nurses, industrial hygienists, and representatives from more than 40 countries. The following aspects on occupational health will be considered:
[illegible]ative methods, medical and surgical prac-
[illegible] and training, social and legal
[illegible] and psychology, environ-
environmental hygiene,
Persons who wish

tion offers grants for the support of the work of established researchers whose studies have a potential relationship to the problems of tuberculosis. The work must be in medicine, sociology, epidemiology, or the basic sciences, and the project must be conducted in an approved university, hospital, or other institution in the New York City area. Applications for fellowships must be made by Nov. 15, while those for grants-in-aid are due at least six months prior to the date when the contemplated project is scheduled to start. Forms may be obtained by writing the New York Tuberculosis and Health Association, 260 Park Ave. South, New York 10.

OREGON

Personal.—Dr. Robert G. Pittenger, Portland, is the new director of the Pacific Northwest Regional Blood Program, succeeding Dr. Bernard Pirofsky, who resigned his post recently to join the staff at the University of Oregon Medical School.——Dr. John A. Benson Jr., recently on the faculty in the department of medicine at Harvard Medical School, Boston, will become associate professor of medicine and head of the division of gastroenterology, University of Oregon Medical School, Portland. He will replace Dr. George B. Long, Portland physician, who has been acting head of the division on a part-time basis for several years. Dr. Long will remain on the faculty as an associate clinical professor.

TENNESSEE

Tennessee Valley Assembly.—On Sept. 28-29, the Tennessee Valley Medical Assembly will be held at the Read House, Chattanooga, sponsored by the Chattanooga and Hamilton County Medical Society. The program includes 17 scheduled papers, among which is "The Decisive Edge," by Dr. Louis M. Orr, Orlando, Fla., president, American Medical Association. Speaker at the banquet, Sept. 28, 7 p. m., will be Dr. Morris Fishbein, professor emeritus (Rush) University of Illinois, College of Medicine, Chicago, who will present "Medicine and the Changing Social Order." Registration fee ($15, payable to Tennessee Valley Medical Assembly) should be sent to Chattanooga Convention and Visitors Bureau, 819 Broad St., Chattanooga, Tenn. The program is approved for category I credit for members of the American Academy of General Practice.

University News.—At the invitation of the department of surgery, Meharry Medical College, Nashville, Dr. George T. Pack, of New York City, delivered the 12th annual Hale-McMillan Lecture April 30. The subject of this lecture was "Sarcomas of the Soft Somatic Tissues."——Feodor Lynen, Ph.D., a biochemist, from Munich, Germany, was the guest of Meharry Medical College March 26-28. His visit was made possible through the courtesy of the Squibb Centennial Lecture Committee.

TEXAS

Southwest Cancer Conference.—The 13th annual Southwest Regional Cancer Conference, sponsored by the Tarrant County Medical Society and the Tarrant County Unit, American Cancer Society, will be held Sunday, Sept. 20, at the Fort Worth Academy of Medicine. Speakers will include, Dr. Shields Warren, professor of pathology, Harvard University; Dr. Eugene P. Pendergrass, professor of radiology, University of Pennsylvania, and Dr. Warren H. Cole, professor of surgery, University of Illinois. For information, write the American Cancer Society, Tarrant County Unit, 264 West 11th St., Ft. Worth, Texas.

UTAH

New Address.—The Utah Tuberculosis and Health Association announced that its new address is Inland Building, 1941 S. 11th E., Salt Lake City 5, Utah (Telephone: INgersoll 6-9101).

VERMONT

University News.—A Ph.D. program in the University of Vermont College of Medicine department of pharmacology has been approved by the university trustees. It is anticipated the program will become effective during the fall of 1959. It becomes the second Ph.D. program at the university.

WEST VIRGINIA

Dr. Boysen Named Child Health Director.—Dr. Theophilus H. Boysen, III, chief of obstetrics and gynecology at Man Memorial Hospital in Man since 1956, accepted an appointment as full-time director of the division of maternal and child health of the State Department of Health. The office in the State Department of Health has remained vacant since Nov. 16, 1956, when the then director, Dr. Helen B. Fraser, resigned to accept a similar post with the Kentucky State Department of Health at Lexington. Prior to becoming a member of the staff of the Man Memorial Hospital, Dr. Boysen engaged in private practice at York, Pa.

Society News.—The West Virginia Academy of Ophthalmology and Otolaryngology in June elected the following officers for the coming year: president, Dr. Nime K. Joseph, Wheeling; president-elect, Dr. John A. B. Holt, Charleston; vice-president, Dr. William K. Marple, Huntington; secretary-treasurer, Dr. Albert C. Esposito, Huntington; director for two years, Dr. James T. Spencer Jr., Charleston. The next meeting will be Aug. 20-23 at the Greenbrier Hotel, White Sulphur Springs.——The officers elected by the West Virginia State Society of Allergy for 1959-1960 are: president, Dr. Sarah L. C. Stevens, Huntington; vice-president, Dr. Marshall J. Carper, Charleston; and secretary-treasurer, Dr. Merle S. Scherr, 803 Atlas Building, Charleston, W. Va.

MISSISSIPPI

Surgeons Meeting in Gulfport.—The Mississippi Chapter of the American College of Surgeons will meet at the Edgewater Hotel Sept. 11-12 at Gulfport. All members of the medical profession are invited. A panel of Dr. Henry W. Scott Jr., Nashville, Tenn.; Dr. Oscar Creech, New Orleans; Dr. James D. Hardy, Jackson; and Dr. Mark C. Wheelock, Chicago, is planned. For information, write Dr. Archibald C. Hewes, president, Mississippi Chapter, American College of Surgeons, Hewes Building, Gulfport, Miss.

MISSOURI

Dr. Wilson Comes to Columbia.—Dr. Vernon E. Wilson, acting dean of the University of Kansas School of Medicine, Kansas City, has been appointed dean of the School of Medicine at the University of Missouri, Columbia. Dr. Wilson will assume his duties Nov. 1. He will succeed Dr. Gwilym S. Lodwick, who has been acting dean of the School of Medicine since Dr. Roscoe L. Pullen resigned the deanship on March 24. Dr. Wilson, chairman of the Governor's Advisory Committee on State Institutions (Kansas), went to the University of Kansas to be assistant dean of the School of Medicine and assistant professor of pharmacology in 1953. In 1957 he was promoted to associate dean and on May 15 of this year, he was appointed acting dean of the School of Medicine and acting director of the University of Kansas Medical Center, to serve until Oct. 15.

NEW HAMPSHIRE

Dr. Weiss Named Psychiatry Chairman.—Dr. Robert J. Weiss assumed the position of professor and chairman of the department of psychiatry, Dartmouth Medical School, Hanover, effective July 1. He resigned his positions in the department of psychiatry, College of Physicians and Surgeons, Columbia University and the Presbyterian Hospital, New York City.

NEW JERSEY

Personal.—Dr. John J. Butler was appointed director of medical education at St. Michael's Hospital, Newark, and associate professor in the department of medicine, Seton Hall College of Medicine and Dentistry. Dr. Butler was formerly director of medical education at St. Mary's Hospital, Rochester, N. Y.——Dr. Selman A. Waksman, co-discoverer of streptomycin and Nobel Prize winner, has retired as director of the Rutgers Institute of Microbiology.

NEW YORK

New York City

Break Ground for New Hospital.—Groundbreaking for the new University Hospital of New York University's medical center took place July 7. Official ceremonies for the founders and friends of the hospital will take place in September. The new 19-story, 600-bed general hospital, to replace the present University Hospital at 303 E. 20th St., will contain a number of special institutes and pavilions—among them the Institute of Neuromuscular Diseases (provided by the Sister Elizabeth Kenny Foundation), the Institute of Reconstructive Plastic Surgery (provided by the Society for the Rehabilitation of the Facially Disfigured), the William J. Wollman Memorial Pavilion for Children, the Lila Motley Radiation Pavilion, the Louis Altschul Cardiac and Hypertension Clinic, the Irvington House Institute for Rheumatic Fever and Allied Diseases, the Milton B. Rosenbluth Diagnostic Clinic, the Julius S. Rippel Laboratories, and the Alfred P. Sloan Radioisotope Laboratory. Construction of the hospital will complete the NYU-Bellevue Medical Center 50-million-dollar development program started in 1948.

Personal.—Dr. Leonard Greenburg, commissioner of the New York City Department of Air Pollution on Control, was elected president of the Air Pollution Control Association.——Dr. Abraham Jablons was elected president of the Alumni Association of the State University of New York Downstate Medical Center in Brooklyn.——Dr. Harvey J. Tompkins, director of the division of psychiatry, St. Vincent's Hospital, was elected president of the Academy of Religion and Mental Health.

Hospital News.—Dr. Ponciano D. Manalo, of Manila, Philippines, was awarded the $500 Travel Fellowship of the Department of Plastic Surgery at the Mount Sinai Hospital, New York City.——Dr. Joseph E. Mule was appointed director of surgery at Saint John's Episcopal Hospital, Brooklyn. Dr. Mule, who received his M.D. at the University of Rome Medical School in 1940, has been on staff of Saint John's Episcopal Hospital since June 30, 1947, and founded the Tumor Registry (accredited by the American College of Surgeons) in 1954. He succeeds Dr. Clarence Dennis, Brooklyn, who recently resigned.

Fellowships for Tuberculosis Research.—Fellowships and grants amounting to $100,000 are being offered by the New York Tuberculosis and Health Association under its recently expanded research program. One of its grants is the James Alexander Miller Fellowship, named in honor of the physician who was one of the organizers and first president of the association. Carrying a stipend of $7,000 to $10,000 depending on need, this fellowship is offered to a "highly qualified" investigator to enable him to pursue research work anywhere in the United States in a field of interest of the association. Candidates who do not receive the Miller Fellowship may be awarded a fellowship carrying a smaller stipend. Priority for these fellowships is given to New York City area applicants. In addition, the association offers grants for the support of the work of established researchers whose studies have a potential relationship to the problems of tuberculosis. The work must be in medicine, sociology, epidemiology, or the basic sciences, and the project must be conducted in an approved university, hospital, or other institution in the New York City area. Applications for fellowships must be made by Nov. 15, while those for grants-in-aid are due at least six months prior to the date when the contemplated project is scheduled to start. Forms may be obtained by writing the New York Tuberculosis and Health Association, 260 Park Ave. South, New York 10.

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TENNESSEE

Tennessee Valley Assembly.—On Sept. 28-29, the Tennessee Valley Medical Assembly will be held at the Read House, Chattanooga, sponsored by the Chattanooga and Hamilton County Medical Society. The program includes 17 scheduled papers, among which is "The Decisive Edge," by Dr. Louis M. Orr, Orlando, Fla., president, American Medical Association. Speaker at the banquet, Sept. 28, 7 p. m., will be Dr. Morris Fishbein, professor emeritus (Rush) University of Illinois, College of Medicine, Chicago, who will present "Medicine and the Changing Social Order." Registration fee ($15, payable to Tennessee Valley Medical Assembly) should be sent to Chattanooga Convention and Visitors Bureau, 819 Broad St., Chattanooga, Tenn. The program is approved for category I credit for members of the American Academy of General Practice.

University News.—At the invitation of the department of surgery, Meharry Medical College, Nashville, Dr. George T. Pack, of New York City, delivered the 12th annual Hale–McMillan Lecture April 30. The subject of this lecture was "Sarcomas of the Soft Somatic Tissues."——Feodor Lynen, Ph.D., a biochemist, from Munich, Germany, was the guest of Meharry Medical College March 26-28. His visit was made possible through the courtesy of the Squibb Centennial Lecture Committee.

TEXAS

Southwest Cancer Conference.—The 13th annual Southwest Regional Cancer Conference, sponsored by the Tarrant County Medical Society and the Tarrant County Unit, American Cancer Society, will be held Sunday, Sept. 20, at the Fort Worth Academy of Medicine. Speakers will include, Dr. Shields Warren, professor of pathology, Harvard University; Dr. Eugene P. Pendergrass, professor of radiology, University of Pennsylvania, and Dr. Warren H. Cole, professor of surgery, University of Illinois. For information, write the American Cancer Society, Tarrant County Unit, 264 West 11th St., Ft. Worth, Texas.

UTAH

New Address.—The Utah Tuberculosis and Health Association announced that its new address is Inland Building, 1941 S. 11th E., Salt Lake City 5, Utah (Telephone: INgersoll 6-9101).

VERMONT

University News.—A Ph.D. program in the University of Vermont College of Medicine department of pharmacology has been approved by the university trustees. It is anticipated the program will become effective during the fall of 1959. It becomes the second Ph.D. program at the university.

WEST VIRGINIA

Dr. Boysen Named Child Health Director.—Dr. Theophilus H. Boysen, III, chief of obstetrics and gynecology at Man Memorial Hospital in Man since 1956, accepted an appointment as full-time director of the division of maternal and child health of the State Department of Health. The office in the State Department of Health has remained vacant since Nov. 16, 1956, when the then director, Dr. Helen B. Fraser, resigned to accept a similar post with the Kentucky State Department of Health at Lexington. Prior to becoming a member of the staff of the Man Memorial Hospital, Dr. Boysen engaged in private practice at York, Pa.

Society News.—The West Virginia Academy of Ophthalmology and Otolaryngology in June elected the following officers for the coming year: president, Dr. Nime K. Joseph, Wheeling; president-elect, Dr. John A. B. Holt, Charleston; vice-president, Dr. William K. Marple, Huntington; secretary-treasurer, Dr. Albert C. Esposito, Huntington; director for two years, Dr. James T. Spencer Jr., Charleston. The next meeting will be Aug. 20-23 at the Greenbrier Hotel, White Sulphur Springs.——The officers elected by the West Virginia State Society of Allergy for 1959-1960 are: president, Dr. Sarah L. C. Stevens, Huntington; vice-president, Dr. Marshall J. Carper, Charleston; and secretary-treasurer, Dr. Merle S. Scherr, 803 Atlas Building, Charleston, W. Va.

Personal.—Dr. Edward J. Van Liere, Morgantown, dean of the West Virginia University School of Medicine, has been elected an affiliate of the Royal Society of Medicine, London, England. The society was founded in 1805 and chartered in 1834.——Dr. Robert P. Hagerman, recently retired from service with the Department of Justice, has been named by Dr. Richard J. Lilly, head of the West Virginia State Department of Mental Health, as superintendent of Weston State Hospital. He succeeds Dr. Lilly, who has served as superintendent during the past several months.

WYOMING

State Medical Election.—Elected officers of the Wyoming State Medical Society are: Drs. Benjamin Gitlitz, Thermopolis, president; Francis A. Barrett, Cheyenne, president-elect; S. J. Giovale, Cheyenne, vice-president; Frederick H. Haigler, Casper, secretary; Carleton D. Anton, Sheridan, treasurer; Albert T. Sudman, Green River, delegate to A. M. A.; and Bernard J. Sullivan, Laramie, alternate delegate to A. M. A.

GENERAL

Change of Address.—Mail intended for the Joint Commission on Mental Illness and Health, its officers, or its staff should be addressed as follows: Joint Commission on Mental Illness and Health, Massachusetts Mental Health Center, 74 Fenwood Road, Boston 15. Following conclusion of the study projects of the National Mental Health Survey on June 30, editorial offices will be maintained at the new address until publication work on the monograph series and final report is complete.

Books for Philippine Medical Library.—A request for medical books and journals from A. M. A. members has been received from Dr. Mercedes V. Planas, of Cebu City, Philippines, for the Cebu Medical Library. The organization, "Books for Asian Students," has agreed to handle the shipping. Publications should be shipped by motor freight, collect (not Railway Express or moving van). The shipment should be addressed to Cebu Medical Library, % Books for Asian Students, 21 Drumm St., San Francisco 11, Calif. Packing in ordinary cardboard cartons tied with rope is sufficient. Packages will be repacked for overseas shipment. Dr. Planas' address is P. O. Box 55, Cebu City, Philippines.

Physicians to Tour Russia.—Six American physicians will begin an exchange mission to Russia on Sept. 5, from Helsinki, Finland. They are Drs. Clifford J. Barborka, Chicago; William B. Castle, Boston; James Murray Luck, Palo Alto, Calif.; Currier McEwen and William H. Sebrell Jr., of New York City; and Floyd S. Daft, of Bethesda, Md. The tour will proceed first to Moscow to visit medical institutes and laboratories and then start a month-long itinerary which will include Leningrad, Sochi, Sukhumi, Kiev, and Odessa. Dr. Barborka, president, American Gastroenterology Association, is taking a previous tour to coordinate a program of medical researches in gastroenterology, which will take him to Sweden, France, Spain, the Netherlands, Germany, England, and Switzerland.

Otorhinolaryngological Congress in Paris.—The 57th French Congress of Otorhinolaryngology will take place Oct. 19-22 in the Grand Amphitheater of the Faculty of Medicine, rue de l'Ecole de Médecine, under the presidency of Dr. Andre Soulas, of Paris, and the honorary presidency of Prof. L. Binet, dean of the Faculty of Medicine of Paris. The program includes presentation of papers, and two reports will be discussed: (1) Surgery for Deafness—Its Present State, Its Future, and (2) The Laryngologist and Actual Data on Treatment of Acute Respiratory Insufficiencies. An exposition of surgical instruments, appliances, and pharmaceutical specialties will be held in the Hall of the Faculty. For information, write the General Secretary, Dr. Henry Guillon, 6, Avenue MacMahon, Paris 17, France.

Research Fellowships and Grants.—The Life Insurance Medical Research Fund is receiving applications for two types of awards to be available July 1, 1960, as follows: (1) Until Oct. 15, 1959, for postdoctoral research fellowships. Candidates may apply for support in any field of the medical sciences. Preference is given to those who wish to work on fundamental problems, especially those related to cardiovascular function or disease. Minimum stipend is $4,500 with allowances for dependents and necessary travel. (2) Until Nov. 1, 1959, for grants to institutions in aid of research on cardiovascular problems. Support is available for physiological, biochemical, and other basic work broadly related to cardiovascular problems as well as for clinical research in this field. Information and application forms may be obtained from the Scientific Director, Life Insurance Medical Research Fund, 345 E. 46th St., New York 17.

Occupational Health Congress in New York.—The 13th International Congress on Occupational Health will be held July 25-29, 1960, at the Hotel Waldorf-Astoria, New York City, organized under the auspices of the International Association on Occupational Health. The program will include physicians, nurses, industrial hygienists, and representatives from more than 40 countries. The following aspects on occupational health will be considered: administrative methods, medical and surgical practices, education and training, social and legal aspects, work physiology and psychology, environmental factors in health, environmental hygiene, and hazards of specific industries. Persons who wish to present papers at the congress should obtain information by writing Dr. Irving R. Tabershaw, Chairman of the Scientific Program Committee, International Congress on Occupational Health, 375 Park Ave., New York City.

Medical Writers' Meet in St. Louis.—The 16th annual meeting of the American Medical Writers' Association will be held at the Chase Hotel, St. Louis, Oct. 2-3, under the presidency of Dr. Morris Fishbein, Chicago. There will be morning, afternoon, and evening sessions on Oct. 2 and a four-hour conference on medical writing the morning of Oct. 3, under the chairmanship of Dr. William D. Snively Jr., of Evansville, Ind. The conference will comprise three sections: Technical Aspects of Medical Writing, Contributions of Other Arts and Sciences to Medical Writing, and Technical Aspects of Publishing and Editing. Over 30 speakers are on the program. A complete program may be obtained from Dr. Harold Swanberg, Secretary, W. C. U. Building, Quincy, Ill. (The meeting will be preceded by the 24th annual meeting of the Mississippi Valley Medical Society at the Chase Hotel, Sept 29-Oct. 1.)

Surgeon Wins Golf Tournament.—Dr. Gerald F. Dederick Jr., Hackensack, N. J., surgeon, won top honors at the American Medical Golfing Association 43rd annual tournament with a low gross total of 69. About 200 physicians teed off in the tourney which was played on two courses at the Seaview Country Club. For Dr. Dederick, it was a repeat performance, since he topped the physician-golfers at the tournament which was held in conjunction with the 1954 A. M. A. annual meeting in Atlantic City. Dr. James O. Smith, general practitioner of Clinton, Mo., had a low net championship with a 64. He shot an 80 and had a 16 handicap. In the senior class (60 and over) Dr. Edward J. Kempf, Wading River, N. Y., shot 81 for low gross honors. Dr. Paul E. Reeves, Scottsville, N. Y., and Francis L. McNelis, Providence, R. I., were winners in the Calloway (undetermined handicap) class. Dr. James C. McLaughlin, Philadelphia, was succeeded as president of the association by Dr. John A. Growden, of Kansas City.

Grants-in-Aid for Nutrition Research.—The National Vitamin Foundation wishes to bring to the attention of those engaged in clinical and basic research in nutrition, biochemistry, and metabolism its current major interest "in the support of research, preferably on man, most likely to advance our understanding of the diverse metabolic functions of the vitamins." Research on vitamin nutrition and metabolism in the areas of (1) mental health and (2) skin eruptions related to drug ingestion and allergies is encouraged, and applications for grants-in-aid of such research from interested and qualified investigators are invited. Application forms may be obtained from the offices of the foundation at 149 E. 78th St., New York 21, N. Y. The foundation takes action on applications twice a year, in the spring and fall. For grants to be effective July 1, applications should be mailed to the foundation before the preceding March 1; for January grants, applications should be in the possession of the foundation by Sept. 15.

Second World Conference on Medical Education.—Medical educators from 55 different countries will take part in the Second World Conference on Medical Education in Chicago, Aug. 20-Sept. 4. The conference is being held under the auspices of the World Medical Association. The collaborating groups include the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities. There will be 125 speakers. Russia is expected to send a delegation to the conference and will have at least two speakers on the program. Poland, another nonmember of the W. M. A., will also send representatives. Dr. Raymond B. Allen, chancellor, University of California, Los Angeles, president of the conference, said, "It is the purpose of this Second World Conference on Medical Education to pass on to the young in mind and heart the experience and learning of the ages. In that way we are advancing the welfare of all mankind regardless of political differences, race, and creed." Dr. Victor Johnson, Rochester, Minn., is deputy president of the conference.

Funds for Health Education.—The National Foundation announced allocations of more than one million dollars in March of Dimes funds for education in the health professions, including an appropriation for a new fellowship program "to give doctors more extensive clinical training in the fields of rheumatology and birth defects." Awards for education in the health fields are in addition to grants made for the same period in research and clinical investigation. The combined sum awarded is more than $3,500,000. The first 515 winners of a health scholarship program initiated earlier this year to provide four-year college training for young Americans in medicine, nursing, physical therapy, medical social work, and occupational therapy will be announced this summer. The fellowship program recently announced is open to residents or practicing physicians for study in rheumatology or in the treatment of patients suffering from birth defects of the central nervous system. Fellowships will be awarded for a minimum period of one year but are subject to renewal. Stipends will range from $3,600 to $7,000 a year. More than $900,000 of the educational grants announced today will go to universities, institutions, and professional associations to support the teaching and recruitment programs.

Dietetic Meeting in Los Angeles.—The 42nd annual meeting of the American Dietetic Association will be held Aug. 25-28 at the Shrine Auditorium, Los Angeles. Staff conferences and meetings will precede the annual meeting. Panel discussions are planned as follows: "A Look at Atherosclerosis Today," with Dr. Laurence W. Kinsell, Oakland, Calif., coordinator; "Spectrums in Various Nursing Programs Today," Miss Marjorie E. Newton, San Francisco, moderator; "What Are Your Needs in Food Packaging and Processing?" Lendal H. Kotschevar, Ph.D., Missoula, Mont., moderator; and "Opportunities for Social Science Research in Dietetics," Edward Wellin, Ph.D., New York City, coordinator. Discussions will also be given under the general title, "Share and Compare," at which several papers will be presented, with one session to be presented each day. Films, exhibits, and group discussions are planned. The annual banquet will be held Aug. 27 at the Statler Hilton Hotel. For information write Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

Society News.—At the meeting of the **Society for Investigative Dermatology** June 6-7, the following officers were elected: Dr. Thomas B. Fitzpatrick, Portland, Ore., president; Dr. Harvey Blank, Miami, Fla., vice-president; Drs. Thomas H. Sternberg, Los Angeles, and Eugene J. VanScott, Bethesda, Md., appointed to board of directors.——The following officers of the **American College of Chest Physicians** were elected for the year 1959-1960: president, Dr. Seymour M. Farber, San Francisco; president-elect, Dr. Mathew J. Flipse, Miami, Fla.; first vice-president, Dr. Hollis E. Johnson, Nashville, Tenn.; second vice-president, Dr. John F. Briggs, St. Paul, Minn.; treasurer, Dr. Charles K. Petter, Waukegan, Ill.; and assistant treasurer, Dr. Albert H. Andrews, Chicago.——The newly elected officers of the **American Neurological Association** are: president, Dr. Derek Denny-Brown, Boston; president-elect, Dr. Harold G. Wolff, New York; first vice-president, Dr. Charles Rupp Jr., Philadelphia; second vice-president, Dr. Samuel Brock, New York; secretary-treasurer, Dr. Melvin D. Yahr, 710 W. 168th St., New York 32; and assistant secretary, Dr. Clark H. Millikan, Rochester, Minn.

Symposium on Tuberculosis Prevention.—A Symposium on the Prevention of Tuberculosis in Children will be held Thursday, Nov. 12, 2 p. m., in the New York Academy of Medicine Building, 2 E. 103rd St., New York City. The Tuberculosis Preventorium for Children at Farmingdale, N. J., is celebrating its 50th anniversary this year, and the symposium, for those interested in the prevention of tuberculosis from a professional and laymen's point of view, is one of the events planned by the 50th Anniversary Committee. Dr. James E. Perkins, New York City, managing director, National Tuberculosis Association, will serve as moderator. Dr. Herbert R. Edwards, associate professor of public health and medicine, Yale University School of Medicine, New Haven, Conn., will discuss "The Role of a Health Department." Dr. Arvid J. Wallgren, emeritus professor of pediatrics, Royal Caroline Medical School, Stockholm, Sweden, will speak on BCG vaccination, and Mrs. Shirley H. Ferebee, associate chief, operational research, tuberculosis program of the U. S. Public Health Service, will discuss chemoprophylaxis. This symposium has been arranged by Dr. Edith M. Lincoln, former head of the Children's Chest Clinic at Bellevue Hospital and a member of the Preventorium Medical Board.

National Association Meeting in Detroit.—The 64th convention of the National Medical Association will be held in Detroit, Aug. 10-13, with the Detroit Medical Society and associated committees as host. Headquarters will be the Sheraton-Cadillac Hotel. Dr. R. Stillmon Smith, Macon, Ga., president of the association, will present and address at the opening session, Aug. 11. A symposium, "Genetics in Modern Medicine," will be given at a joint session, Aug. 11, and the section meetings will include the following symposiums and moderators:

The Current Place of Adrenal Cortical Steroids in Medical Practice, Dr. Walter L. Henry Jr., Washington, D. C.
Recent Advances in the Diagnosis and Treatment of Rheumatic and Collagen Diseases, Dr. Everett N. Rottenberg, Detroit.
Newer Trends in the Diagnosis and Treatment of the Common Anemias, Dr. Allison B. Henderson, Detroit.
Recent Advances in the Diagnosis and Treatment of Peripheral Vascular Insufficiency, Dr. Homer M. Smathers, Detroit.
Recent Advances and Management of Congestive Heart Failure, Dr. William Gibson, Detroit.
Some Practical Approaches to the Diagnosis and Management of Pulmonary Insufficiency, Dr. Audley R. Mamby, Chicago.
Newer Concepts in Ophthalmology and Otolaryngology, Dr. Howard P. Venable, St. Louis.
Carcinoma of the Uterus, Dr. William F. Goins, Detroit.
The Importance of Early Diagnosis—Cancer, Tuberculosis, Venereal Diseases, Dr. Edith Irby Jones, Hot Springs National Park, Ark.

A clinical pathology conference is planned for Aug. 13. Round-table discussions, panel discussions, and scientific and technical exhibits are planned. There is no registration fee. A ladies' program is arranged. For information, write Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Rehabilitation Fellowship for Latin American.—The World Rehabilitation Fund in cooperation with the International Society for the Welfare of Cripples announced the creation of the Bell Greve Memorial Fellowship, created to honor the memory of the late Miss Bell Greve, Cleveland, who for many years served as secretary-general, International Society for the Welfare of Cripples. The Bell Greve Memorial Fellowship will be given to a trainee from Latin America for a minimum of one year's training in rehabilitation in the United States. The fellowship may be given to a physician, physical therapist, occupational therapist, prosthetist, orthotist, speech and hearing therapist, or rehabilitation counsellor. Miss Greve headed a Red Cross child health center in Czechoslovakia and then moved to Armenia to run an orphanage caring for 4,500 children. After World War I she took a leave of absence as director of the Cleveland Rehabilitation Center to join the staff of UNRRA to establish a rehabilitation service in Greece. At the time of her death in 1957, she was director of public health and welfare, City of Cleveland. Information concerning applications for the Bell Greve Memorial Fellowship may be secured by writing the International Society for the Welfare of Cripples, 701 First Ave., New York 17, or the World Rehabilitation Fund, 400 E. 34th St., New York 16.

Hospital Meeting in New York.—The 61st annual meeting of the American Hospital Association will be held Aug. 24-27, in the New York City Coliseum. General assembly speakers will include Dr. Marcolino G. Candau, Switzerland, director-general of the World Health Organization; Mr. Elmo Roper, public opinion analyst; Mr. Francis Boyer, chairman of the board of Smith Kline and French Laboratories; and Dr. Alexander D. Langmuir, Atlanta, Ga., chief, Epidemiology Branch, Communicable Disease Center, U. S. Public Health Service. Sessions will cover such topics as providing and financing health care for the aged, future of prepayment plans for hospital care, progressive patient care, governing board's responsibility for medical care in the hospital, auxiliary and the hospital service story, evaluating in-hospital volunteer services, hospital school of nursing education, and the hospital and allied health professions. There will be 36 instructional sessions concerned with specific phases of hospital operation. Dr. Leona Baumgartner, commissioner of health for New York City, will speak at the Auxiliary's breakfast Aug. 24, with Dr. Francis J. Braceland, psychiatrist-in-chief, Institute of Living, Hartford, Conn., speaking at the luncheon Aug. 26. General Alfred M. Gruenther, president, American National Red Cross, will be the speaker for the Federal Hospital Executives Luncheon Aug. 25. An International Dinner and the President's Luncheon are scheduled. Allied groups meeting in conjunction with the association's annual meeting will be the American Association of Hospital Consultants, Aug. 22; the American Association for Hospital Planning, Aug. 22-23; the American College of Hospital Administrators, Aug. 22-24; and the American Association of Nurse Anesthetists, Aug. 24-27. About 500 exhibits of new equipment and supplies and educational displays are planned.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	July 4, 1959		July 5, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	1
Rhode Island	..	..	..
Connecticut	..	..	1
Middle Atlantic States			
New York	4	4	3
New Jersey	..	1	1
Pennsylvania	..	..	1
East North Central States			
Ohio	..	3	..
Indiana	2	2	1
Illinois	..	..	..
Michigan	3	6	1
Wisconsin	..	1	2
West North Central States			
Minnesota	..	..	..
Iowa	18	39	..
Missouri	9	16	1
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	6	11	1
Kansas	1	3	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	2	2	1
West Virginia	..	..	2
North Carolina	2	3	1
South Carolina	..	1	..
Georgia	8	10	1
Florida	3	3	8
East South Central States			
Kentucky	1	1	1
Tennessee	2	3	2
Alabama	5	5	1
Mississippi	3	5	5
West South Central States			
Arkansas	6	6	1
Louisiana	6	9	4
Oklahoma	..	7	3
Texas	9	15	12
Mountain States			
Montana	..	..	3
Idaho	..	..	..
Wyoming	1	1	..
Colorado	..	1	..
New Mexico	4	4	1
Arizona	1	1	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	1	..
Oregon	2	2	1
California	8	9	2
Alaska	..	..	..
Hawaii	..	..	4
Puerto Rico	..	..	..
Total	106	175	66

FOREIGN

Congress on Obstetrics and Gynecology.—On Sept. 19-22, a Congress on Gynecology and Obstetrics will be held in Lisbon. The program will include an international meeting of the Portuguese Society of Obstetrics and Gynecology, Sept. 19-20. Subjects for Sept. 19 include "Problems of Diagnosis Presently in Discussion in Relation to Cancer of the Uterus (Cervix and Endometrium)" and "Prophylaxis of Abortion." The fourth congress of the International Professional Union of Gynecology and Obstetrics will be held Sept. 21-22, with the opening session at the Santa Maria Hospital. Two discussions will be devoted to the detection of genital cancer of women from the economic and social point of view. Other themes include "Criterion and Procedures of the Specialization of Gynecology and Obstetrics" and "Economic Classification of Fees and Actions in Obstetrics and Gynecology According to a Scale of Values." A general assembly is planned for 5 p. m., Sept. 22, with the banquet planned for that evening at 8:30 p. m. A ladies' program and a schedule of tours are arranged.

Postpone Congress of Nephrology.—The organizing committee of the first International Congress of Nephrology has announced that it has been obliged to postpone the congress to Sept. 1-3, 1960. The congress was originally scheduled to be held Sept. 3 (in Geneva), and September 4-5 (in Evin), 1959.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application was May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certificates, new and reopened, Part I, and requests for re-examination Part II are now being accepted. *Part I. Written.* Jan. 15, 1960. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1959. No applications can be accepted after that date. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Oral.* St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pathology: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application was March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: Chicago, Oct. 19-20; New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application is July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application was July 1. *Oral.* September. Final date for filing application was July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Abbott, Charles Franklin Ⓜ Syracuse, N. Y.; College of Physicians and Surgeons, Baltimore, 1903; for many years practiced in Elmira, where he was on the staffs of St. Joseph's and Arnot-Ogden hospitals, and associated with the Pennsylvania Railroad; died in the General Hospital May 2, aged 83.

Alexander, Horace Quincy, Russells Point, Ohio; Pulte Medical College, Homeopathic, Cincinnati, 1897; served as mayor; for many years justice of the peace of Washington Township; died in Sarasota, Fla., May 10, aged 88.

Baird, Perry Cossart Jr., Detroit, Mich.; Harvard Medical School, Boston, 1928; served on the faculty of his alma mater; formerly on the staff of the Peter Bent Brigham Hospital in Boston; died May 4, aged 55.

Baker, Robert E. Ⓜ Orleans, Ind.; University of Louisville (Ky.) Medical Department, 1892; member of the American Academy of General Practice; died May 3, aged 97.

Balaban, Joseph S., Boston; University of Istanbul Medical Faculty, Turkey, 1919; for many years medical examiner for the Irish-American Athletic Association, sponsor of amateur fights; died in the Pratt Diagnostic Hospital May 11, aged 69.

Bone, Oscar Lasley, Newark, Ark.; Memphis (Tenn.) Hospital Medical College, 1908; died May 18, aged 74.

Boyes, Henry Robert Ⓜ Detroit; Detroit College of Medicine and Surgery, 1916; during World War I served in France with the American Expeditionary Force; for many years medical missionary in the Middle East, serving as director of the Kennedy Memorial Hospital of the Presbyterian Church in Tripoli, Lebanon, from 1921 until May, 1958; in 1946 received the Gold Medal of the Lebanese Order of the Cedar for his medical services to the people of the nation; died in the Harper Hospital May 9, aged 69.

Brazda, Adolph William Ⓜ Ranger, Texas; born in Dodge, Neb., Jan. 11, 1899; Emory University School of Medicine, Atlanta, 1929; past-president of the Eastland County Medical Society; member of the American Trudeau Society, Southern Medical Association, Association of Military Surgeons of the United States, New York Academy of Science, Texas Academy of Science, Phi Chi Medical Fraternity, and the American Association for the Advancement of Science; received the "Certificate of Merit" in 1958, an international award, for the outstanding paper in the International Academy of Proctology, of which he was a fellow; city health officer for Ranger for three terms; member of the American Legion and the Veterans of Foreign Wars; veteran of World War II, received the EAME Campaign Medal with two Battle Stars; in 1956 promoted to lieutenant colonel in the U. S. Air Force Reserve and retired in January, 1959; a Ranger General Hospital board member for six years, serving one term as board chairman; past-president of the Ranger Rotary Club; died May 20, aged 60.

Brent, Charles Maurice Ⓜ Niagara Falls, N. Y.; born in Mahone Bay, N. S., Canada, Jan. 27, 1904; University of Buffalo School of Medicine, 1929; member of the Radiological Society of North America; past-president and secretary of the Niagara County Medical Society; past-president of the Niagara Academy of Medicine; for three terms president of the board of education, of which he became a member in 1948; from 1939 to 1950 served on the board of directors of the Niagara County Tuberculosis and Health Association; member and past-president of the staff of Mount St. Mary's Hospital, where he died May 3, aged 55.

Briggs, Edward Fitch Ⓜ Truro, Mass.; Baltimore Medical College, 1906; fellow of the American College of Surgeons; veteran of World War I; served on the staff of the Northern Westchester Hospital in Mount Kisco, where he was instrumental in organizing the medical board; died May 21, aged 75.

Briggs, Guy Young, St. Louis; Washington University School of Medicine, St. Louis, 1908; served on the faculty of his alma mater; died in St. John's Hospital May 17, aged 82.

Brown, Frank Eugene, Portland, Ore.; Creighton University School of Medicine, Omaha, 1927; formerly a member of the Portland Boxing Commission; veteran of World War II; served as a member of the medical staff of the Veterans Administration; died in St. Vincent's Hospital May 9, aged 56.

Bruning, Henry Frederick Ⓜ Brooklyn; Columbia University College of Physicians and Surgeons, New York City, 1905; a founder of the Bay Ridge Hospital; on the courtesy staff, department of medicine, Methodist Hospital, where he died May 11, aged 76.

Buczynski, Charles Casimir Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1929; member of the Industrial Medical Association; vet-

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Ⓜ Indicates Member of the American Medical Association.

eran of World War II and the Korean War; on the staff of the Loretto Hospital; died in St. Mary of Nazareth Hospital May 22, aged 55.

Burkes, De Witt Clinton Ⓜ Portland, Ore.; born March 11, 1887; University of Louisville (Ky.) Medical Department, 1911; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association and the Portland Academy of Medicine; fellow and life member of the American College of Physicians; past-president of the Oregon Neuropsychiatric Society; member of the International League Against Epilepsy and the Portland Psychiatrists in Private Practice; for 14 years a member of the Oregon State Board of Health, of which he was vice-president and twice president; past assistant surgeon and surgeon in the U. S. Public Health Service Reserve; veteran of World War I; head of psychiatry at Army Induction Center during World War II; since 1930 clinical associate in psychiatry at the University of Oregon Medical School; medical officer in charge of Veterans Administration at Fort Steilacoon, Wash., from 1921 to 1924 and American Lake, Wash., from 1924 to 1927; staff member, Holliday Park Hospital, Good Samaritan Hospital, St. Vincent's Hospital, and the Morningside Hospital; consultant, Veterans Administration Hospital and the Multnomah Hospital; founder and first president of the Portland Chamber Orchestra; died May 16, aged 72.

Burkhead, Jesse DeWitt Ⓜ Opelika, Ala.; Tulane University School of Medicine, New Orleans, 1920; died in the Wheeler Hospital in La Fayette May 1, aged 65.

Butterfield, Elmore Everest, Long Island City, N. Y.; born in Washington, D. C., in 1881; Columbian University Medical Department, Washington, D. C., 1903; from 1904 to 1906 instructor in pathology at the University of Michigan in Ann Arbor; for the next three years studied at the University of Munich in Germany, where he served as a volunteer assistant in the university's clinical medical institute; under grants from the Rockefeller Institute for Medical Research, worked at the University of Tubingen in Germany and the University of Leiden in the Netherlands; assistant in physics and chemistry at the Rockefeller Institute in New York City from 1911 to 1914; pathological chemist at Bellevue Hospital in New York City, 1914-1915; from 1915 to 1918 pathological chemist and chemist of the central testing laboratory, Bureau of Contract Supervision, City of New York; for many years chemist in charge of physical and the chemical testing laboratory of the Borough of Queens, President's Office, City of New York; died in the Elmhurst (N. Y.) General Hospital May 16, aged 77.

Carter, Henry Rose, Ashland, Va.; University College of Medicine, Richmond, 1897; veteran of the Spanish-American War; died May 13, aged 84.

Charbonneau, Arthur Ames Ⓜ Green Bay, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; veteran of World War I; died May 2, aged 74.

Clark, Lambert Oran Ⓜ Lafayette, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; in 1937 was presented with the 1936 civic cup award for outstanding service to the community by the Young Men's Business Club; surgeon in chief and one of the original members of the board of directors of the Lafayette Sanitarium, where he died May 8, aged 79.

Clay, Calvin Ⓜ St. Charles, Mo.; Washington University School of Medicine, St. Louis, 1922; past-secretary of the St. Charles County Medical Society; veteran of World War I; city physician for six years; recently awarded a selective service medal for uncompensated medical service; served as local physician for Missouri, Kansas and Texas Railroad; formerly on the staff of St. Francis Hospital in Washington, Mo.; on the staff of the St. Joseph's Hospital in St. Charles, where he died May 15, aged 64.

Clifford, Robert Henry Ⓜ Detroit; born in Brooklyn Feb. 10, 1915; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1940; interned at the Union Memorial Hospital in Baltimore, where he served a residency; interned at the Jefferson Hospital in Roanoke, Va.; served a residency at the Presbyterian Hospital in New York City and the Veterans Administration Hospital in New York City; specialist certified by the American Board of Plastic Surgery; fellow of the American College of Surgeons; member of the American Society for Surgery of the Hand and the American Society of Plastic and Reconstructive Surgery; veteran of World War II; physician in charge, division of plastic surgery, Henry Ford Hospital; died in Boston May 15, aged 44, while attending a meeting of the American Association of Plastic Surgeons.

Coleman, John F., Smoaks, S. C.; Medical College of Georgia, Augusta, 1902; died in St. Joseph's Hospital, Savannah, Ga., May 1, aged 83.

Connelly, Leo Augustine, Baldwin, N. Y.; University of Buffalo School of Medicine, 1924; veteran of World War II; served on the staffs of the Cornwall (N. Y.) Hospital and St. Luke's Hospital in Newburgh; died in the Veterans Administration Hospital, Northport, May 2, aged 61.

Cowles, Dwight, Forge Village, Mass.; Tufts College Medical School, Boston, 1913; veteran of World War I; for many years physician for the board of health and school physician in Westford; mill physician of the Abbot Worsted Company of Forge Village; on the courtesy staff of Lowell General Hospital in Lowell, where he died May 15, aged 66.

Cozzens, James Patrick Ⓜ Cleveland; St. Louis University School of Medicine, 1924; supervisor of health service in city public schools; died in the Cleveland Clinic Hospital May 2, aged 61.

Desparois, Guy Bernard Ⓜ Los Angeles; Northwestern University Medical School, Chicago, 1907; on the staff of the Queen of Angels Hospital, where he died May 12, aged 76.

Dorsey, Francis Patrick Jr. Ⓜ Hartington, Neb.; Northwestern University Medical School, Chicago, 1928; past-president of the Cedar–Dakota–Dixon–Thurston–Wayne Counties Medical Society; staff member of Sacred Heart Hospital in Yankton, S. D., and St. Joseph's Hospital in Sioux City, Iowa, where he died May 14, aged 57.

Edlavitch, Baruch Mordecai Ⓜ Fort Wayne, Ind.; Johns Hopkins University School of Medicine, Baltimore, 1910; veteran of World War I; past-president of the Allen County Medical Society; associated with Lutheran and St. Joseph's hospitals, and the Parkview Memorial Hospital, where he died May 18, aged 74.

Fash, James Cone Ⓜ Galesburg, Ill.; University of of Illinois College of Medicine, Chicago, 1940; interned at Missouri Baptist Hospital in St. Louis; served a residency at the Milwaukee County Hospital in Milwaukee and the Methodist Hospital of Central Illinois, Peoria; member of the American Academy of General Practice; veteran of World War II; associated with St. Mary's and Cottage hospitals; died May 11, aged 45.

Fedko, Waldemar Theodore Ⓜ Gordon, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1926; served as secretary of the Pennsylvania Physical Therapy Association; for eight years Schuylkill County coroner; physician for the Schuylkill County Prison in Pottsville; secretary of the staff of Ashland (Pa.) State Hospital; served on the staff of the Frankford Hospital in Philadelphia; past-president of the Ashland Rotary; died in Pottsville (Pa.) Hospital May 13, aged 58.

Feider, Arnold Peter Ⓜ Cleveland, Wis.; Marquette University School of Medicine, Milwaukee, 1944; member of the American Academy of General Practice; veteran of World War II; staff member of the St. Nicholas and Memorial hospitals in Sheboygan and Holy Family and Memorial hospitals in Manitowoc; died in Sheboygan May 9, aged 39.

Fink, Elizabeth Ⓜ Bridgeport, Conn.; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1923; died May 20, aged 69.

Goldstein, Abraham Ⓜ Lakewood, N. J.; Long Island College Hospital, Brooklyn, 1911; past-president of the Ocean County Medical Society; associated with the Paul Kimball Hospital, where he was past-chief of staff; died May 27, aged 71.

Gonda, Victor Emanuel Ⓜ Palo Alto, Calif.; born in Hungary May 7, 1889; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1911; specialist certified by the American Board of Psychiatry and Neurology; member of the American Academy of Neurology, American Psychiatric Association, and the Central Neuropsychiatric Association; past-president of the Chicago Neurological Society; formerly practiced in Chicago, where he was on the faculty of Rush Medical College, Loyola University School of Medicine, and Cook County Post Graduate School; served on the staffs of Cook County Hospital, and Alexian Brothers Hospital in Chicago; associated with the Veterans Administration Hospital; died in the Palo Alto Hospital May 17, aged 70.

Gradwohl, Rutherford B. Hayes Ⓜ St. Louis; born in Baltimore March 4, 1877; Washington University School of Medicine, St. Louis, 1898; member of the American Urological Association and the American Academy of General Practice; in 1954 received an award from the American Academy of Forensic Science, of which he was founder; veteran of World War I; later rose to the rank of commander in the U. S. Naval Reserve; director of the crime laboratory of St. Louis Police Department; for many years director of the Gradwohl School of Laboratory Technique and the Gradwohl Laboratories; formerly instructor of pathologic anatomy at St. Louis University School of Medicine and professor of bacteriology at Barnes Medical College; served as coroner's physician for many years; at one time laboratory director and member of the pathology and bacteriology staffs at St. Louis County Hospital; for many years pathologist at the Christian Hospital; at one time editor of the *Bulletin of St. Louis Medical Society;* author of "Blood and Urine Chemistry" and "Clinical Laboratory Methods and Diagnosis"; died in the Jewish Hospital May 9, aged 82.

Gulledge, John F. Ⓜ Siloam Springs, Ark.; University of Louisville (Ky.) Medical Department, 1889; died May 16, aged 94.

Gunn, Aubrey Jackson Ⓜ Versailles, Mo.; Barnes Medical College, St. Louis, 1904; died May 8, aged 78.

Hall, Ralph Marsh Ⓜ Cold Spring, N. Y.; Albany (N. Y.) Medical College, 1915; veteran of World War I; associated with the Julia L. Butterfield Memorial Hospital, where he was a trustee; died May 21, aged 67.

Heard, E. Felton, Goree, Texas; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1902; died in Dallas May 12, aged 81.

Hemler, William Francis, Tampa, Fla.; Georgetown University School of Medicine, Washington, D. C., 1904; at one time on the faculty at his alma mater and the Georgetown Hospital in Washington, D. C.; died May 11, aged 80.

Ingber, Irving Samuel Ⓜ San Francisco; Long Island College Hospital, Brooklyn, 1913; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; veteran of World War I; head of the radiology department, Mary's Help Hospital; died in the Mills Memorial Hospital in San Mateo, May 18, aged 70.

Jaques, Jefferson Singleton, St. Louis; University of West Tennessee College of Medicine and Surgery, Memphis, Tenn., 1915; died in the Koch Hospital May 17, aged 73.

Jernstrom, Roy E. Ⓜ Rapid City, S. D.; born in Escanaba, Mich., Sept. 23, 1896; University of Minnesota Medical School, Minneapolis, 1923; past-president of the South Dakota State Medical Association; Black Hills District Medical Society and Rapid City Medical Society; member of the American Fracture Association; fellow of the International College of Surgeons and the American College of Surgeons; served as president of the school board of Rapid City; veteran of World War I; medical member of the Selective Service Board from 1941 to 1945; associated with the Bennett-Clarkson Memorial and St. John's McNamara hospitals; died in Rochester, Minn., May 11, aged 62.

Keeney, Cadwell Benson Ⓜ Summit, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1907; veteran of World War I; on the Selective Service Board during World War II; past-president of the city board of health; for many years on the staff of the Overlook Hospital; received the Golden Merit Award of the Medical Society of New Jersey for half a century of service; died May 22, aged 77.

Keil, Charles A., New York City; Fordham University School of Medicine, New York City, 1918; member of the Industrial Medical Association; died May 19, aged 68.

Keller, Jacob Adlai, Chesterfield, Mass.; Columbia University College of Physicians and Surgeons, New York City, 1905; member of the board of health and served as school physician; associated with the Cooley Dickinson Hospital in Northampton, where he died May 11, aged 79.

Lanier, Louis Fielding Ⓜ Sylvania, Ga.; Medical College of Georgia, Augusta, 1910; associated with the Screven County Hospital, where he died May 11, aged 81.

Lee, John Gordon Ⓜ Washington, D. C.; born in Edmonton, Alta., Canada, June 7, 1902; McGill University Faculty of Medicine, Montreal, Que., Canada, 1928; member of the American Association for the Surgery of Trauma; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; veteran of World War II; clinical adjunct professor of surgery at Georgetown University School of Medicine and adjunct clinical professor of surgery at George Washington University School of Medicine; interned at the Royal Victoria Hospital in Montreal, Que., Canada, and the Presbyterian Hospital in New York City; served a residency at the Lakeside Hospital in Cleveland, Bellevue Hospital in New York City and the Free Hospital for Women in Brookline, Mass.; chief of surgical service, Veterans Administration Hospital (Mount Alto); died at his home in Silver Spring, Md., May 9, aged 56.

Leopold, Albert Reid Ⓜ Lewistown, Pa.; University of Pittsburgh School of Medicine, 1927; served as secretary and president of the Mifflin-Juniata Counties Medical Society; for many years member and chairman of the board of health; associated with the Lewistown Hospital; died in the Presbyterian Hospital, Pittsburgh, May 9, aged 57.

Little, Albion Henry, Portland, Maine; Medical School of Maine, Portland, 1899; served in France during World War I; past-president of the Cumberland County Medical Society; associated with the Maine Eye and Ear Infirmary; died in Yarmouth May 16, aged 82.

Lo Vene, Arthur Wilhelm, Galesburg, Ill.; Illinois Medical College, Chicago, 1908; associated with the Mercy Hospital in Burlington, Iowa; died in Peoria April 14, aged 76.

Magrish, Philip Ⓜ San Antonio, Texas; University of Cincinnati College of Medicine, 1934; specialist certified by the American Board of Pediatrics; fellow of the American Academy of Pediatrics; past-president of the San Antonio Pediatric Society; veteran of World War II; associated with Santa Rosa Hospital, Baptist Memorial Hospital, and Nix Memorial Hospital; died May 11, aged 50.

Maxson, Frank Theodore Ⓜ Seattle; University of Pennsylvania Department of Medicine, Philadelphia, 1902; veteran of World Wars I and II; for many years associated with the city fire department and in 1957 was honored by the city council for his service; past-president of the King County Medical Society; member of the Association of Military Surgeons of the United States; on the staffs of the

Providence, Doctors, Swedish, and Seattle General hospitals; died in the Veterans Administration Hospital May 20, aged 79.

McClements, William Montgomery Ⓜ Pittsburgh; Jefferson Medical College of Philadelphia, 1935; veteran of World War II; on the staff of the Magee Hospital; died May 17, aged 52.

McKinley, Arthur O., Salisbury, Pa.; College of Physicians and Surgeons, Baltimore, 1894; died in the Meyersdale (Pa.) Community Hospital May 4, aged 91.

McLean, Sterling Alexander Ⓜ Middleboro, Mass.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1934; medical examiner of the Fourth District, Plymouth County; veteran of World War II; secretary of the staff of St. Luke's Hospital; died May 16, aged 50.

Milburn, Azby Alexander Ⓜ Weston, W. Va.; Medical College of Virginia, Richmond, 1927; member of the American Psychiatric Association; associated with the Weston State Hospital; died May 18, aged 59.

Miller, Clay O. Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1926; served on the faculty of Stritch School of Medicine of Loyola University; veteran of World Wars I and II; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the International College of Surgeons and the American College of Surgeons; on the staff of Henrotin Hospital; consultant, Veterans Administration Hospital, Hines, Ill.; chairman of the department of urology at West Suburban Hospital in Oak Park, where he died May 24, aged 61.

Moore, Harry Beaumont, Portland, Ore.; Jefferson Medical College of Philadelphia, 1913; died May 19, aged 71.

Muttart, George Wheelock Ⓜ Jersey City, N. J.; University of the City of New York Medical Department, New York City, 1892; served on the staffs of the Christ, Fairmount, and Greenville hospitals; died in New York City May 16, aged 92.

Newbill, James Ⓜ Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1941; member of the American Society of Anesthesiologists; past-president of the Arkansas Society of Anesthesiology; veteran of World War II; on the staff of the Arkansas Baptist Hospital; died May 10, aged 45.

Paganelli, Joseph Erpinio Ⓜ Staten Island, N. Y.; Long Island College Hospital, Brooklyn, 1917; veteran of World Wars I and II; served on the staffs of the New York Eye and Ear Infirmary and the Veterans Administration Hospital in New York City; associated with St. Vincent's and Staten Island hospitals; associate attending physician at the Richmond Memorial Hospital, where he died May 23, aged 68.

Pellens, Mildred, Bridgeport, Conn.; Cornell University Medical College, New York City, 1930; member of the American Psychiatric Association; served on the staff of the Bridgeport Hospital, where she died May 1, aged 62.

Richards, Lloyd Hildrique, Phoenix, Ariz.; St. Louis College of Physicians and Surgeons, 1901; formerly associated with the Indian Service; died May 5, aged 83.

Rosenbaum, Louis Ⓜ New York City; George Washington University School of Medicine, Washington, D. C., 1927; fellow of the American College of Chest Physicians; formerly on the faculty of Columbia University College of Physicians and Surgeons; veteran of World War II; examining physician for the department of health and chief of consultation chest service at the Harlem Health Center; on the staffs of the Harlem, Lincoln, and Riverside hospitals; died in the Mount Sinai Hospital May 16, aged 57.

Ross, William Edson Ⓜ Jacksonville, Fla.; University of Vermont College of Medicine, Burlington, 1904; past-president of the Florida Medical Association; served on the staff of St. Luke's Hospital; died May 16, aged 80.

Shepler, Robert MacMurran Ⓜ Carlisle, Pa.; Jefferson Medical College of Philadelphia, 1902; fellow of the International College of Surgeons and the American College of Surgeons; past-president of the board of health of Carlisle; associated with the Carlisle Hospital; died May 12, aged 85.

Spahr, Mary Burchard Ⓜ Ithaca, N. Y.; Cornell University Medical College, New York City, 1922; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; on the staff of the Tompkins County Memorial Hospital; died May 25, aged 62.

Spurney, Paul Marcus Ⓜ Cleveland; Western Reserve University School of Medicine, Cleveland, 1917; veteran of World War I; for many years health officer of Shaker Heights; fellow of the International College of Surgeons; for many years chief of staff of the Polyclinic Hospital; died in the Lakeside Hospital April 25, aged 66.

Stites, Thomas Henry Atherton Ⓜ Nazareth, Pa.; born in Wyoming, Pa., April 26, 1875; University of Pennsylvania Department of Medicine, Philadelphia, 1901; veteran of the Spanish–American War; fellow of the American College of Physicians; member of the American Trudeau Society; served as president, vice-president, and secretary of the Northampton County Medical Society; at one time associated with the Pensylvania State Health Department as medical inspector of dispensaries; served with the U. S. Public Health Service Reserve, on the staff of the U. S. Public Health Service Hospital No. 26 in Greenville, S. C., on the staff of the U. S. Public Health Service Hospital No. 27 in Alexandria, La., medical director of the Pennsylvania State Sanatorium for Tuberculosis No. 2 in Cresson, Pennsylvania State Sanatorium for Tuberculosis No. 3 in Hamburg, and attending physician at the West Mountain Hospital in Scranton; formerly vice-president of the First National Bank and past-president of the Rotary Club in Cresson, Pa.; past-president of the Nazareth Rotary Club; for many years editor of the Bulletin of the *Northampton County Medical Society;* died May 23, aged 84.

Storkan, Joseph Charles Ⓜ Gardena, Calif.; Creighton University School of Medicine, Omaha, 1914; veteran of World War I; served as mayor of Plentywood; associated with the Las Campanas Hospital, Compton, where he was past-president of the medical staff; died in St. Mary's Hospital, Long Beach, May 12, aged 72.

Tirrell, John Mahlon, Minneapolis, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1900; died in the Doctors Memorial Hospital April 26, aged 83.

Townsend, Arthur Melvin Sr., Nashville, Tenn.; Meharry Medical College, Nashville, 1902; served on the faculty of his alma mater; died April 20, aged 83.

Tucker, Edmond D. Ⓜ Nutter Fort, W. Va.; College of Physicians and Surgeons, Baltimore, 1907; member of the staff of St. Mary's Hospital in Clarksburg; died May 17, aged 79.

Vocale, Antonio, Chicago; Regia Università degli Studi di Pavia. Facoltà di Medicina e Chirurgia, Italy, 1940; interned at Mother Cabrini Memorial Hospital; died in April, aged 50.

Voris, Henry McMunn Ⓜ Stuart, Fla.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; for many years practiced in East St. Louis, Ill.; veteran of World War I; died April 26, aged 80.

Wagner, George Garfield Jr. Ⓜ Gowanda, N. Y.; *University of Buffalo School of Medicine, 1929;* member of the American College of Chest Physicians and the American Trudeau Society; served on the staff of the J. N. Adam Memorial Hospital in Perrysburg; died April 16, aged 53.

Wiley, George Adrian Ⓜ Norman, Okla.; Northwestern University Medical School, Chicago, 1933; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; assistant professor of ophthalmology at the University of Oklahoma School of Medicine in Oklahoma City; associated with University Hospitals in Oklahoma City and the Norman Municipal Hospital; died April 27, aged 54.

Wolf, Heinrich Franz Ⓜ New York City; born in Bistrau, Austria, Sept. 23, 1872; Deutsche Universität Medizinische Fakultät, Prague, Austria, 1897; specialist certified by the American Board of Physical Medicine and Rehabilitation; instructor in physical medicine at Columbia University College of Physicians and Surgeons from 1910 to 1932; member and past-president of the New York Society of Physical Medicine; member of the American Association for the Advancement of Science; fellow of the New York Academy of Medicine and the American Congress of Physical Medicine; co-founder and director of the Eastern School for Physicians' Aides; consultant at the Mount Sinai Hospital, where in 1910 he was appointed chief of the department of physical medicine, a position he held until 1932; from 1932 to 1938 attendant director of physical medicine at the Central Neurological Hospital; author of "A Textbook of Physical Therapy," "Shortwave and General Electrotherapy," "The Practice of Physical Medicine," and "Philosophy for the Common Man"; died while vacationing in Seville, Spain, May 12, aged 86.

Wolfer, Henry Ⓜ Monterey, Mass.; University and Bellevue Hospital Medical College, New York City, 1908; specialist certified by the American Board of Internal Medicine; fellow of the American *College of Physicians; from 1942 to 1944* clinical professor of medicine at the Long Island College of Medicine in Brooklyn, where he was at one time instructor and assistant clinical professor of medicine; formerly associated with the Cumberland Hospital in Brooklyn; served as consulting physician at the Kings County Hospital and the Long Island College Hospital in Brooklyn; died May 23, aged 73.

Wronker, Benno M., New York City; Columbia University College of Physicians and Surgeons, New York City, 1909; died May 26, aged 73.

Yamada, So Sabro, Los Angeles; Stanford University School of Medicine, San Francisco, 1922; member of the American Trudeau Society; died in the Japanese Hospital Feb. 27, aged 68.

Zaff, Fred Ⓜ New Haven, Conn.; University of Michigan Medical School, Ann Arbor, 1937; assistant clinical professor of radiology at Yale University School of Medicine; specialist certified by the American Board of Radiology; veteran of World War II; member of the American College of Radiology; associated with the Veterans Administration Hospital in West Haven; radiologist at the Grace-New Haven Community Hospital, where he died March 12, aged 47.

FOREIGN LETTERS

AUSTRIA

Congenital Dislocation of the Hip.—At the meeting of the Austrian Pediatric Society in Vienna in April Dr. P. Erlacher reported that the classic method of treatment for congenital dislocation of the hip, as devised by Lorenz in 1895, has undergone various modifications. Lorenz recommended that repositioning not be attempted before the 2nd year of life, but it has been recognized that this procedure can be accomplished more easily when the child is younger. It is, therefore, important to diagnose the dislocation as early as possible. With the help of roentgenograms the diagnosis can be established even in the nursing infant, and in these patients a cure is possible by simple means. One of the earliest signs is "snapping" of the joint. Treatment in infancy can be accomplished without anesthesia and without a plaster cast.

In Czechoslovakia, where the incidence of dysplasia and dislocation of the hip is higher than in Austria, pregnant women are cautioned against the dangers of dysplasia in their expected infants. They are informed that by broad swaddling and by the application of the abduction cushion or abduction linen described by Frejka a mild degree of dysplasia may be cured and dislocation thus prevented. As a rule roentgenograms of all infants are obtained at the age of 3 months. The roentgenograms are read by an experienced orthopedist, and infants with abnormal findings are treated.

The speaker considered routine roentgenography necessary only in suspected cases. In the course of this development forceful passive reduction and fixation in a plaster cast have gone out of use in Czechoslovakia. A. Pavlik has achieved spontaneous reduction without the use of force not only in the preliminary stages of dislocation and partial dislocation but also in those with definite dislocation, with the aid of strap-reins. He left it to the child's natural impulse to movement to accomplish spontaneous reduction without external force. The strap-reins extend along the legs to the heel and as suspenders over the shoulders. They are adjusted in a somewhat rectangular positioning of the legs. Otherwise all movements are unrestricted. Frequently with this treatment the tension in the abductors is relieved within a few days, abduction becomes free, and the dislocation suddenly disappears. Pavlik has used this method for mild cases since 1945, and since 1951 also for fully developed dislocations. For best results this method should be used between the 8th and 9th weeks of life, but it may be successful at any time in the 1st year. Of 1,795 dislocations treated by this method spontaneous reduction was obtained in 1,664 or 92.7%. If one adds the patients in preliminary stages and those with partial dislocation, 4,674 hips were treated by this method. The speaker stressed the fact that rebuilding of the head of the femur has not yet been observed. The strap-reins do not interfere with the treatment of intercurrent diseases. This method was used at the orthopedic hospital in Vienna for the last year and Pavlik's experiences with the method were confirmed in 70 patients. Particularly impressive was the case of a 6-month-old girl with arthrogryposis, congenital rigidity of limbs, club hand, and talipes. Such patients are considered particularly hard to treat and some physicians refuse even to attempt to treat the dislocation. Spontaneous reduction was achieved within six weeks in this infant with the aid of the strap-rein.

Broad swaddling is recommended for the prevention of any kind of dysplasia. Infants should not be swaddled upward, with the thighs together, but their thighs should be placed as much as possible in abduction and swaddling cloth, longitudinally folded, led from the back over the buttocks to the abdomen and fixed with a second swaddling cloth or a swaddling ribbon. Over this the straddle-pouch is placed. For the treatment of preliminary stages, partial dislocation, and every dislocation, with or without "snapping," Pavlik's strap-reins are used to achieve spontaneous reduction. The straps are placed on the naked legs extending to the heels and are securely fixed to the suspenders, which are crossed over the back and are worn over the shirt like those used for leather shorts. This is done with hips and knees placed at an angle of more than 90 degrees. After a few days the straps can be removed when the infant is bathed. It is advisable to mark the position of the foot portions of the strap carefully. After reduction has been accomplished the strap-reins should be worn for at least as long as a plaster cast would have been worn with the old treatment. Although the method is simple, roentgenographic follow-up is still necessary. Redislocation was observed in six children, but in two this was due to faulty technique. All children who by the age of 3 months have not obtained a cure should be referred to an orthopedist.

The items in these letters are contributed by regular correspondents in the various foreign countries.

BRAZIL

Gastroscopy.—Pontes and Meirelles reviewed a series of 400 gastroscopies in 346 patients (*Rev. paulista med.* 54:15, 1959). Comparing the gastroscopic with the radiologic and surgical findings, the authors classified these patients as those in whom (1) gastroscopy confirmed the clinical and radiologic diagnosis (102 patients); (2) gastroscopy confirmed a tentative clinical and radiologic diagnosis (29); (3) gastroscopy revealed a lesion in addition to that diagnosed radiologically (18); (4) the correct diagnosis was established by gastroscopy alone (99); (5) gastroscopy invalidated an earlier radiologic diagnosis and established a correct one, later confirmed by operation or new radiologic examination (43); (6) gastroscopy did not contribute to the diagnosis and in some cases even confused the clinical reasoning, since it aroused an erroneous diagnostic suspicion (17); (7) gastroscopy led to an erroneous diagnosis (12); (8) gastroscopy was inconclusive because some food remained in the stomach (13); (9) the diseased areas could not be observed because they were situated in so-called blind spots (6); and (10) the gastroscope could not be introduced into the stomach (7). Thus of the 346 patients examined gastroscopy was of diagnostic aid in 291 or 84.1% (the patients in the first 5 categories). Gastroscopy was of particular value in the diagnosis of certain forms of gastritis. It was also of help in the differential diagnosis of peptic ulcer or cancer.

Laryngoscopy of the Subglottis.—In the examination of the larynx, the subglottic region is always left unexplored, as the vision in this field is restricted, if not impossible. Dr. F. Freire, of the São Paulo State University Hospital, devised a technique for examining this region by retrograde laryngoscopy which he reported to the Associação Paulista de Medicina. With use of six anatomic preparations the examination was begun by puncturing the trachea through the linea alba of the neck, the apparatus being introduced through the laryngotracheal ligament, between the cricoid cartilage and the first tracheal ring. When loss of resistance occurred, meaning that the instrument had entered the tracheal lumen, the mandril was pulled out and an antrorhinopharyngoscope was introduced until the tracheal mucosa was visible.

By inclining the external part of the instrument the lenses and the light were pointed craniad, showing all the subglottis. By pushing the apparatus toward the subglottic dome it was possible to see the anterior and the posterior commissures, the lower surfaces of the vocal cords, and the vocal apophyses of the arytenoid cartilages. Pushing further through the glottis, it was possible to see the lower surface of the ventricular bands corresponding to the interligamentous glottis, part of the ventriculus laryngis, and the foot of the epiglottis. In all six preparations the aspects were the same. Thus, having proof of the feasibility of the procedure, Dr. Freire, using the same technique, examined an 81-year-old man who had carcinoma of the hypopharynx and the larynx to determine what parts should be resected. As a consequence of the retrograde examination it was decided not to perform a resection but to apply roentgenotherapy.

Artery Used to Replace Ureter.—J. L. Itiberê and co-workers, of the São Luís Gonzaga Hospital of Jaçanã, São Paulo, encouraged by their results in using arteries preserved in alcohol to replace blood vessels, tried them as replacements for the ureter. They reported their results to the Associação Paulista de Medicina. Aortas of dogs, preserved in 48% alcohol for 22 to 215 days at room temperature, were used as replacements for the right ureter in 13 dogs. The ureter was severed about 4 cm. from the pelvis of the kidney, its distal stump being tied with cotton thread. The proximal stump was introduced into the arterial lumen, the ureter being maintained in its new position by the fixation of the upper end of the preserved artery to the retroperitoneal fat and the adjacent peritoneum, which was folded over the prosthesis, thus filling the space resulting from the difference in diameter between the artery and the ureter. The prosthesis was then peritonized. Soon after the operation the dogs received 400,000 units of penicillin intramuscularly. In four dogs a left nephrectomy was performed before the grafting in order to ascertain the value of the prosthesis, and postoperative excretory urography was performed in eight. Five dogs died 3, 4, 6, 15, and 150 days after operation, all but one from causes attributable to the operation. Eight dogs were alive 33 to 164 days after the operation, and of these three had previously had a nephrectomy.

DENMARK

BCG Vaccination of School Children.—A law passed in 1946 provided for the annual medical examination for tuberculosis not only of every school child but also of every teacher and the school staff in general. Dr. K. Bojlen (*Ugeskrift for laeger,* April 2, 1959) reported that the percentage of positive tuberculin reactors at the school-entry age in Copenhagen from 1937 to 1957 fell from 17.4 to 3.9. Encouraging as these figures are, they show that during the first seven years of life a child may still become infected. Between 1944 and 1957 50 members of the school staff were found to have active pulmonary tuberculosis. The author's proposed remedy for this state of affairs is a more systematic program of BCG vaccination as early as possible in the scholastic curriculum. Once children are thus vaccinated before entering school it should be possible to follow them closely in this respect throughout their scholastic careers. The author recommended that the routine practice of giving newborn infants in maternity hospitals BCG vaccination be revived. This was done in one such hospital in 1950, and may have contributed to the fall in the percentage of positive tuberculin reactors in 1957.

Poliomyelitis Vaccination.—The State Serum Institute in Copenhagen issued a memorandum on poliomyelitis vaccination. A series of four injections will be given free of charge to anyone under 18 years of age. As paralytic cases have occurred in quite young children, the lowest age limit has been brought still further down, and the vaccine can now be given to children aged only 4 or 5 months, but as infants are poor antibody-makers, because their mothers have transmitted antibodies to them, it is well to reduce the interval between each injection to one month. After the age of 1 year the interval between the first and second injection should be four to six weeks, between the second and the third injection from 9 to 12 months, and between the third and fourth injection about one year. When in doubt about spacing of doses it is better to overdo than to underdo vaccination. The poliomyelitis vaccine and the diphtheria-tetanus toxoid can be given on the same day.

Stillbirth Rates.—Prof. D. Baird of the University of Aberdeen spoke on stillbirths at a meeting of the Danish Gynecological and Obstetric Society (*Ugeskrift for laeger*, April 9, 1959). He stated that in 1956 Denmark had a stillbirth rate of 17 per 1,000 births, whereas the corresponding rate for England and Wales was 23. The figures for Scotland also point to the relative superiority enjoyed in this respect by Denmark. The stillbirth rate appears to be correlated with the cesarean section rate, as in Denmark it is about one-third of that for England. The reason why the Danes have achieved better results with simpler means, with regard to stillbirths, than the English and the Scottish may, in Baird's opinion, be found in the better average physique of Danes. The mean height of Danish women is much greater than that of their Scottish sisters. This may be because of the agricultural life led by the Danes, who have been spared the slums created by an industrial mode of life.

Cancer Propaganda and Tobacco Smoking.—In the *Danish Medical Bulletin* for March, 1959 (vol. 6), Dr. A. Nörgaard traced the influence of fear of cancer on the consumption of tobacco. Toward the end of 1953 the Danish newspapers carried on an exhaustive debate on the alleged effects of cigarette smoking on the lungs, with special reference to cancer. To measure the reaction to this debate questions were addressed during the first four months of 1954 to 4,260 male and 2,089 female smokers. The answers showed that only 158 (3.7%) men and 90 (4.3%) women had stopped smoking altogether. These figures can, however, be made to look more impressive by applying them to the whole of Denmark, with the calculation that had this census been conducted on a national scale about 46,000 men and 28,000 women would have changed their smoking habits and 5,800 men and 3,200 women would have ceased to smoke altogether in response to the debate.

Arterial Transplants.—Dr. P. A. Gammelgaard and co-workers (*Ugeskrift for laeger*, March 19, 1959) stated that in the sterilization of dry-frozen blood vessels in the artery bank ethylene oxide has been replaced, because of its explosive properties and irritant effect on mucosa, by a penicillin-streptomycin mixture. Bacteriological and histological tests were made directly after excision, after sterilization, and after dry-freezing. Although the supply to the artery bank was taken from persons under the age of 40 years whose deaths had occurred less than 48 hours earlier, the samples discarded on account of such degenerative changes as atherosclerosis amounted to 35%. On a follow-up examination six months to two years after operation 13 of 17 patients who had by-pass transplantations had satisfactory results, whereas thromboses had occurred in the others. In view of the legal difficulties arising from the employment of human graft material the search for artificial substitutes has been intensified. Ivalon has been shown to undergo certain structural changes and to become too stiff in the human body. Crimped Teflon promises to be a satisfactory successor by virtue of the facility with which it can be handled and the retention of its best qualities in the human body, in which it is biologically inert.

FINLAND

Relapses After Surgery for Pulmonary Tuberculosis.—O. Peräsalo and co-workers (*Ann. chir. et gynaec. Fenniae* 48:1-18, 1959) made a follow-up study of a series of 527 tuberculous patients who were treated surgically between 1949 and 1957. Statistics on the 273 subjected to thoracoplasty showed that after an observation period of one and one-half to eight years primary and secondary cures were obtained in 71.2%, and 15.9% were still ill. Primary surgical mortality accounted for 2.5% and late tuberculous complications proved fatal in 8.6%. The data on 96 patients subjected to pneumolysis showed that, with an observation period varying from two and one-half to eight years, the percentage of primary and secondary cures was 83.4 and 12% were still ill. Primary surgical mortality was 2.1% and mortality from late tuberculous complications was 2.5%. The follow-up studies on 153 patients operated on by pulmonary resection showed that, after an observation period of six months to six years, the proportion of cures was 90.2% and 3.3% were still ill. Primary surgical mortality was 3.9%, and the mortality from late tuberculous complications was 2.6%. The relapse rate in patients with extensive cavitation was 55.3% after thoracoplasty and 46.7% after pneumolysis. Most of these relapses, however, occurred after the thoracoplasties and pneumolyses performed between 1949 and 1952, when the new drugs were not yet routinely used. In analyzing the type of resection used no major differences were apparent between the groups of those who had lobectomy, lobectomy plus segmental resection, and segmental resection alone. Their relapse rates were 13.4 to 11.4%. There were no relapses after pneumonectomy or polysegmental resection.

Surgery in Aged Persons.—Viikari and Vaalasti (*Ann. chir. et gynaec. Fenniae* 48:19-30, 1959) reviewed a series of 565 operations performed on persons over 70 years of age. Of these 72 were over 80 years of age. The total postoperative mortality was 11%, 9% for those under and 22% for those over 80. The mortality after emergency operations was 21%, that after operations with absolute indications 15%, and that after elective operations 5%. The chief causes of postoperative death were embolism, cardiac failure, and pneumonia. The author stressed the need for appropriate preoperative management of patients in order to diminish postoperative complications. In patients in whom a curative measure was in question, such as those with enlarged prostate, severe pains caused by biliary calculi, and hernia, the decision was usually easily made, for modern anesthesia increases the chances of a favorable outcome. The situation is more difficult if a malignant tumor is involved and a radical operation is necessary. The life of a person aged 70 to 80 may not be agreeable if, for example, the whole stomach or a lung is removed, however successfully. The life of such a patient would not be appreciably lengthened and as a result of the operation his last years might be much more difficult than they would be if the operation had not been performed.

GERMANY

Hypergammaglobulinemia.—Kühn and Hanusch reported, at the 65th meeting of the German Society of internal medicine at Wiesbaden in April, that 55% of 3,000 paper electrophoreses showed an increase of the gamma globulin fraction of more than 40%. Most of these were from patients with severe subacute and chronic hepatitis, cholangitis, hepatic cirrhosis, tumors (chiefly leukemia), and inflammatory diseases of the heart, lungs, and pleura. The gamma globulin deflection showed, with few exceptions, a broad base, and, especially in hepatic diseases, was asymmetric. In seven patients the gamma globulins were arranged in a more or less sharply pointed fraction with a narrow base; only one of these was a true gamma plasmocytoma. Patients with acute inflammatory and neoplastic diseases usually showed an increase of serum protein–bound carbohydrates in the rapidly moving range, while those with chronic inflammatory diseases, especially of the liver, also showed a large portion of serum protein–bound carbohydrates in the range of the increased gamma globulin fraction.

Antirheumatic Drugs and Hyaluronidase.—At the same meeting H. Mathies of Munich stated that previous studies had shown that the hyaluronidase-inhibiting effect of antirheumatic drugs was bound to the function of the adrenal medulla (release of catecholamine). An activity of the adrenal cortex can be proved, but it does not play a role in the process of hyaluronidase inhibition. Release of catecholamine from the adrenal medulla was indirectly proved by determination of the catecholamine content of the adrenals after administration of various antirheumatic drugs and treatments. Intensive studies showed that antirheumatic agents are of two classes. One kind (salicylates and glucocorticoids) affect the release of catecholamine mainly at the expense of the normal adrenal depots; the other (phenylbutazone and estrogens) give rise to an increase in the production of catecholamine, and a surplus of this is then released.

The inhibition of hyaluronidase does not take place during the primary period of effect of catecholamine but only after its subsidence. Intensive work on the dependence of hyaluronidase inhibition on the catecholamine effect has already been done. It depends not on the time of catecholamine release but on the time of decline of the previously elevated catecholamine level. These findings suggested that the release of catecholamine starts a reactional process that requires further clarification. From the spreading effect achieved with a dyestuff plus hyaluronidase applied to rats and human beings it was seen that protamine sulfate blocks the hyaluronidase-inhibiting effect of heparin and all other antirheumatic substances possessing this property. The inhibition of hyaluronidase by epinephrine, levarterenol, histamine, and all other hyaluronidase-inhibiting substances and treatments (salicylates, phenylbutazone, adrenocortical hormones, chlorethylbenzmethoxazone, mud baths, and sulfur baths) is blocked by ergotamine tartrate and by antihistaminics. Not only ergotamine tartrate but also ganglionic blockers block the inhibition of hyaluronidase.

Polysaccharide Content of Fibrin.—At the same meeting J. Rechenberger of Leipzig reported that carbohydrates are present as integral parts in the serum protein bodies under both physiological and pathological conditions. This polysaccharide portion increases in most pathological conditions. Only in diseases of the liver parenchyma were the levels found to keep within the normal range or to be only slightly elevated. A certain polysaccharide portion is also always found in fibrin. Fibrin was prepared from oxalate plasma by means of thrombin. With the orcin reaction and a modified Elson-Morgan test it was possible to demonstrate in various conditions that the polysaccharides hexosen and hexosamine were present in varied amounts, depending on the underlying disease. High polysaccharide levels were associated with tumors, especially bronchial carcinoma, and in such inflammatory diseases of the lung as lobar pneumonia. In diabetes, especially if attended by complications, the polysaccharide portion was increased, markedly in some patients, parallel to the increase of fibrin nitrogen. Investigations further suggested that carbohydrates were closely linked with the synthesis and perhaps also the function of the fiber material.

Hepatitis Contagiosa Canis.—At the same meeting Mohr and Schindler of Hamburg stated that viral hepatitis in a dog (hepatitis contagiosa canis) was first described by Rubarth in 1947. The causative organism is identical with that of fox encephalitis, discovered by Green in foxes in 1925. In 1933 Green experimentally investigated the pathogenicity of this virus for dogs. While in the fox the infection takes the course of an encephalitis, in the dog it is characterized by hepatitis. The report that ferrets and rabbits are susceptible to this virus has not been proved. Recent reports, however, indicated a possibility of transmission to monkeys, which suggested that human beings might become infected.

The observation of an attack in a veterinarian caused the authors to investigate whether the virus of hepatitis contagiosa canis might be pathogenic for man. Two more human cases were observed in the veterinarian's environment, and these also showed more or less marked symptoms and a high serologic titer for this infection. Liver swelling was the most characteristic symptom. Liver biopsy performed in another clinic, regrettably only toward the final stage of the disease, revealed histological indications of a noncharacteristic irritation of the liver tissue, with swellings of Kupffer's cells and an increase mainly of eosinophils in the lobular sinusoids. Liver function tests also showed slight deviations. From then on, one of the authors investigated serums of patients with hepatitis in the clinic and also serums from patients suspected of having psittacosis, toxoplasmosis, or undefined viral infection.

The serums were examined for hepatitis contagiosa antibodies by the complement-fixation reaction. Two positive reactions were obtained. In one it was too weak to permit any evaluation, but in the second a marked titer deviation was observed. The latter was in a serum that had been sent for diagnosis because of undefined viral infection. This patient had had contact with cats and dogs. On the first day of the disease an itching rash had been observed that spread over the whole body on the second day. The patient's temperature was subfebrile. He had conjunctivitis, bronchitis, and swellings of the cervical, buccal, axillary, and inguinal lymph nodes. The leukocyte count was 2,300 with an increase of plasma cells and monocytes. The sedimentation rate was increased. A follow-up examination after four months confirmed subsidence of all symptoms, and at that time the result of the serologic test had become negative. The report pointed out that people in close contact with dogs may acquire this viral infection. It may run a mild course with only minor involvement of the liver, or it may develop as a severe disease with hepatic involvment.

Absorption of Orally Taken Penicillin.—A. Lange and co-workers (*Arzneimittel-Forschung*, vol. 9, 1959) determined the blood levels of healthy volunteers after oral administration of 100,000 and 200,000 units of phenoxymethyl penicillin (PV), 100,000 and 200,000 units of potassium phenoxymethyl penicillin (PVK), and a combination of 100,000 units each of PV and PVK. In the PV-treated group receiving 100,000 units (23 subjects) three types of reaction were observed: maximum values occurring after one hour (early-level group, 8 subjects); two hours (middle-level group, 10 subjects); and four hours (late-level group, 5 subjects). With double the dose there was a greater portion of early levels: 11 early, 3 middle, and 2 late levels. In the PVK-treated group receiving 100,000 units (15 subjects) peak levels occurred in 13 subjects after only one hour, because of the more rapid absorption of the potassium penicillin; only 2 subjects had middle levels. All of 15 subjects receiving 200,000 units of PVK had early levels. The values obtained with the combination of 100,000 units of PV and 100,000 units of PVK in 18 subjects were surprising. The ratio of early to late levels was 14:2, but, contrary to expectation, peak levels were higher than after 200,000 units of PV or 200,000 units of PVK. Also the values after four hours were clearly higher than those from 200,000 units of PV. The comparatively great range of values was due to individual differences in decomposition, excretion, and distribution of the orally taken penicillins. Body weight, which also contributes to the divergence of values was not considered in these tests.

Pseudoarthritis After Withdrawal of Prednisone.—Dölle and Martini (*Med. klin.* 53:2177, 1958) reported that steroid pseudoarthritis with fatigue, diffuse muscle and joint pain, and psychic lability is especially likely to develop in women during the menopause after long-term corticosteroid treatment of primary chronic rheumatoid arthritis. The authors observed the same syndrome in three women in the menopause after sudden termination of prednisone treatment for idiopathic liver cirrhosis. Joint pain predominated in the first and polyneuritic symptoms in the two others. Physical therapy and treatment with salicylic acid (of differential diagnostic importance) had no effect. Treatment therefore consisted of gradual reduction of the prednisone dosage until its complete withdrawal. If the pseudorheumatism occurs after termination of the hormone treatment, prednisone should be reinstituted in low and gradually declining doses, until it is finally withdrawn.

Separation of Urinary 17-Ketosteroids.—At the 65th meeting of the German internal medicine society at Wiesbaden in April, Heni and Göbel of Tubingen stated that separation by paper chromatography of the 17-ketosteroids in urine into their components is important in the differential diagnosis of hypercorticoidism. A method was worked out which allows satisfactory but easy separation of androsterone, etiocholanolone, dehydro-epiandrosterone, 11-keto-androsterone, 11-keto-etiocholanolone, 11-hydroxy-androsterone, and 11-hydroxy-etiocholanolone. The method was used in the examination of several forms of adrenocortical hyperfunction. Separate demonstration of metabolites from androgens and cortins (within the 17-ketosteroid fraction) permits more definite conclusions of the type of adrenocortical dysfunction than was possible with the previously used group reactions of the urinary corticoids or with adsorption chromatography to alumina.

In the purely metabolic form of pituitary basophilism only an increase in such metabolites of cortisone as etiocholanolone, 11-keto-etiocholanolone and 11-hydroxy-etiocholanolone is found. In the mixed forms an increase in 11-keto-androsterone and 11-hydroxy-androsterone is also observed. Adrenal hirsutism with elevated 17-ketosteroid values is associated with an increase in dehydro-epiandrosterone, 11-hydroxy-androsterone, and androsterone. The clinical difficulties in the differential diagnosis of uncomplicated hirsuties without elevation of the 17-ketosteroid levels are relieved further by administration of ACTH. In adrenocortical dysfunction, increased excretion of metabolites from androgens is observed. This is absent when the condition is of extra-adrenal origin. Congenital forms of the adrenogenital syndrome, which are characterized by disturbances of the synthesis of steroid hormones, show an increase in 11-hydroxy-androsterone, while the level of dehydroepiandrosterone is only slightly elevated.

Absolute Arrhythmia.—At the same meeting Franke and Stein reported on a series of 900 patients with a critical inflammatory or degenerative myocardial disease, valvular heart disease, or thyrotoxicosis and absolute arrhythmia. Only about 10% of the patients complained of cardiac irregularities. About 50% of those with valvular heart disease and 25% of those with myocardial disease had cardiac decompensation. The most frequent arrhythmia was auricular fibrillation. Pure auricular flutter was observed in only 5%. In 80% of the patients the electrocardiogram (ECG) showed further signs of damage and 23 of 46 patients with paroxysmal absolute arrhythmia had a pathological ECG during the rhythmic phases. The average age of the patients with valvular heart disease was lower than that of the others, and twice as many had a history of embolism. Among the patients with valvular heart disease many had manifest cardiac failure and roentgenographically demonstrable auricular dilatation. Of the 80 patients receiving quinidine regular rhythm was established for lengthy periods in 16.

Secondary Renal Insufficiency.—At the same meeting J. Frey of Freiburg reported that in diabetics increasing glucosuria (up to 150 Gm. per day) was accompanied by a steady increase in urinary volume and sodium, chloride, potassium, and phosphate excretion. The excretion of urea was less affected and creatinine excretion hardly at all. The concentration of urine was only slightly increased and with further sugar excretion returned to aglucosuric values. The speaker further stated that diabetic coma was a special form of functional kidney damage which might be associated with marked chloride and sodium deficiency and other electrolyte changes in the plasma, such as hyperkalemia and hypokalemia. Because of the higher excretion of urates and of morphologic changes of the kidneys resulting in gross deposits of urates in the kidneys in gout, renal function is impaired. The concentrating power of the kidneys is impaired and the excretory power reduced, with the exception of urate clearance which is only slightly altered if at all and during the gouty attack may even be increased. In Fanconi's rachitic syndrome it is difficult to distinguish renal and extrarenal conditions, since this syndrome is not an anatomic but a clinical entity. The associated phosphaturia leads to osteomalacia. The prognosis is better in adults than in children.

INDIA

Tetracycline for Typhoid.—Parikh and Thanawala (*Journal of the Indian Medical Association*, vol. 32, April 16, 1959) gave tetracycline alone and in combination with chloramphenicol to 189 patients with typhoid. Salmonella typhosi in vitro was found to be sensitive to between 0.25 and 31.2 mcg. of tetracycline and in vivo to 10, 30, and 60 mcg. of tetracycline. The patients were treated by five regimens: (1) 30 were given 500 mg. of tetracycline every 4 hours; (2) 29 received 500 mg. of tetracycline every 6 hours; (3) 40 were given both 250 mg. of tetracycline and 250 mg. of chloramphenicol three times a day; (4) 28 were given 750 mg. of chloramphenicol twice a day for three to four days, followed by 750 mg. of tetracycline twice a day; and (5) 3 patients with severe toxemia received 500 mg. of tetracycline intravenously twice daily until their temperatures came down to normal; 2 of these were then given chloramphenicol by mouth and one was given tetracycline by mouth. The control group of 59 patients received 1.5 Gm. of chloramphenicol per day. The dosage in all the test groups was reduced gradually after the temperature touched normal, and therapy was continued for 7 to 10 days. If tetracycline failed to bring the temperature down to normal within 7 or 8 days, chloramphenicol was given.

Treatment was started in most of the patients on the 7th to 13th day of fever. There was no significant difference in mortality in those receiving tetracycline alone or chloramphenicol alone. The most remarkable effect of tetracycline was the clearing up of the toxemia. Most of the patients' conditions became nontoxic within 48 to 72 hours, although their temperatures remained above normal. As the patients improved they became more cooperative, and this helped in maintaining nutrition and in rapid recovery. The general weakness so often complained of in convalescence was also absent in patients treated with tetracycline. Chloramphenicol gave satisfactory results in patients who proved refractory to tetracycline. The results in the group receiving both drugs simultaneously were much better than in the control or any other group. Patients who received tetracycline alone or in combination with chloramphenicol were relieved of toxemia earlier than those who received chloramphenicol first and then tetracycline or chloramphenicol alone. The duration of stay in hospital was less in those receiving combined therapy. Both drugs were well tolerated, there being hardly any side-effects. The two drugs given in combination also helped to reduce the carrier state.

Viruses from Sporadic Cases of Meningitis.—S. Paul and co-workers (*Journal of the Indian Medical Association*, vol. 32, April 16, 1959) studied a sporadic series of 27 patients who had encephalitis, with a view to isolating viruses from the stools. Eight healthy children and seven with febrile illness other than encephalitis or aseptic meningitis were included as controls. Samples of stool, cerebrospinal fluid, and blood were examined. Blood specimens in the convalescent state were collected 14 days after the onset of illness. From healthy children and patients with other febrile illness, only stool specimens were collected. All specimens were subjected to tissue culture, mouse inoculation, neutralization tests, and tests for virus isolation. Fourteen cytopathogens were isolated, 13 from stools and 1 from cerebrospinal fluid. Ten were isolated in cultures from patients with encephalitis, aseptic meningitis, or both and two in those from normal healthy children. No such pathogens were isolated in cultures from the seven with febrile illness other than encephalitis. Cultures from one patient with encephalitis yielded two cytopathogens, one from the stool and the other from the cerebrospinal fluid.

All patients with encephalitis had low-grade pyrexia and 10, 2 of whom had paralysis, showed signs of involvement of the central nervous system. Two developed residual paralysis, one died, and the rest recovered. Five samples of cerebrospinal fluid showed pleocytosis, three showed a moderately low sugar level, two increased protein levels, one decreased chloride levels, and two were normal. Only one showed leukocytosis. Results of mouse inoculation tests showed 4 of the 14 cytopathogens to be pathogenic in mice. Neutralization tests showed that of the 14 strains studied 3 were poliovirus 1, one was poliovirus 2, two were poliovirus 3, two were Coxsackie virus B5, 6 could not be neutralized by any of the poliovirus or Coxsackie virus serums used, and of these 6 only 4 could be neutralized by gamma globulin. None of the tested strains were neutralized by pooled monkey serum. The two poliovirus 1 strains were isolated from patients with paralysis or paresis, and one of these had residual paralysis of the lower limb. Poliovirus 3 and Coxsackie virus B5 came from patients with aseptic meningitis. One of these strains was isolated from the cerebrospinal fluid of the patient whose stool cultures yielded poliovirus 2. None of the Coxsackie virus strains were isolated from healthy children.

JAPAN

Fall-out from Nuclear Tests.—A special committee headed by Dr. Totugi and appointed by the Atomic Energy Commission measured the fall-out of radioactive matter in and around Japan in 1957 and the first half of 1958. The fall-out showed a definite cumulative increase with each successive year. In the localities heaviest hit it is fast approaching a dangerous level. Japan seems to receive a heavy fall-out of radioactive dust from all directions—specifically from Eniwetok in the Pacific, from Nevada in the United States, from Siberia, and even from the North Pole. The tests of rain water for radioactive strontium (Sr^{90}) showed more than 8 $\mu\mu$c. In 1956 1 sq. km. in Tokyo contained 2 μc of Sr^{90}. In 1958 it had increased to 12 μc. In 26 separate areas the water supply contained Sr^{90} in a dangerous concentration. Every test of foods grown on the soil showed a high level of Sr^{90}, the most notable being that found in rice. Fortunately, most of it is removed in the millings of the grain; but these heavily charged millings are fed to the live stock whose dairy products and meats are later eaten. We do not yet know whether the Sr^{90} ingested in food and water ultimately reaches the bones. It is estimated that the amount of Sr^{90} ingested daily is 2.03 $\mu\mu$c by the urban and 5.8 $\mu\mu$c by the rural population. If to the above figures we add those for heavily laden drinking water and the unpolished rice used by some we reach a dangerously high daily dose of 26 $\mu\mu$c.

CORRESPONDENCE

A PHILOSOPHY OF MEDICINE

To the Editor:—The time-honored meaning of the word physician is under close scrutiny. We need an immediate and a long-range philosophy of medicine. The immediate needs must come from within the profession. There must be unity in principles, unity in action, and unity of dedication to the fundamental motivations and principles that facilitated the emergence of medicine as a great science.

The motivation of the physician today will have tremendous impetus on the future of medicine. If our primary motivations are knowledge of disease, understanding of the patient, and treatment of the patient, we shall remain true physicians, humanitarians, and practitioners of the healing art. But when our primary motivation revolves around economics, we are in trouble. The latter motivation is then subject to legislation, controls, third-party intervention, and numerous alien impacts on the patient-physician relationship. The large increase in number of malpractice suits against doctors and hospitals proves that the old-time patient-physician relationship is shattered and that courts must now intervene to settle complaints. The person-to-person relationship between patient and physician becomes broken, and the right of preferred information is in jeopardy. Intervention by a third party breaks the most sacred and cherished privilege of medicine, the right to privacy. Great damage can be inflicted on a patient's ego by legislated method and management of his personal history. The physician management of medical care is changing, and this alone has hurt the valuable proved personal relationship which can exist between patient and doctor.

The American way of life is changing, and we must take cognizance of it in any philosophy. Federal legislation relating to medicine is a reality. State legislation providing medical care is increasing. The politicians, the labor leaders, the industrialists, and the insurance companies are now engaged in the administration of American medicine. These basic inroads into the private practice of medicine have been occurring for many years. It is a myth that bureaucratic medicine is cheaper and better than the private practice of medicine. Someone will pay for the operation of political medicine, and in the end it will be the patient—with his life—and the doctor—with his self-respect.

Our immediate reaction to the changes in medical practice are diversified. The medical profession is divided. There are advocates who wish to cooperate with coercion and who accept and promote various agencies and medical programs without investigation or intelligent critical examination. This encourages governmental legislation, facilitates the creation and centralization of medical bureaucracy, and contributes to the policy that leads to the ultimate socialization of medicine and enslavement of both the patient and doctor.

There are physicians who advocate compromise; they say that change is inevitable and that the needs of the people must be met. At the same time they attempt to preserve the private practice of medicine. They study numerous proposals and advocate various schemes that will impress the people and placate the physicians. They affirm freedom of choice of a physician, freedom in rendering medical judgments, and freedom in the pursuit of medical knowledge. The basic fallacy of compromise is third-party intervention, the application of nonmedical judgments, and costly benefits appropriated to the advocates who pretend to render cheaper medical care. You may be sure that when insurance companies write policies they have profit in mind.

There are physicians who advocate open resistance to change. These rugged individualists, staunch adherents to private enterprise, oppose the encroachment on their personal liberty, judgment, and exercise of duty. Freedom is an American heritage and should be allowed to exist between patient and doctor. But the balance of power, greed, and ignorance are against advocates of individual freedom, who lack support from within their profession, are legislated into piecemeal curtailments, and, as individuals, cannot stop the mounting entanglements and inroads being imposed on medical practice. A united approach, rather than individualistic pronouncements, would be more effective.

Our immediate action is diversified. The cooperators endorse, the compromisers negotiate, and the traditionalists oppose intervention. This divided state of opinion leads to chaos; medicine becomes contaminated, and an era of decline will be inaugurated producing the typical decadent socialist-motivated type of doctor.

The long-range view of future medicine requires substantial agreement on a philosophy of medicine. Without an adequate philosophy, we flounder, we opinionate, we wait, we surrender our gains to the politician, the labor leader, and the medical moron. From within the profession must come a unified concept of medical practice, a united approach of combating destructive influences, and a presentation of a constructive program which will insist as well as prove that physicians are able to manage the health and welfare of American medicine and the American people.

History has demonstrated that the greatest advances in medicine occur when medicine becomes the prerogative of the physician. Medicine belongs to trained physicians, not to politicians, insurance companies, or labor leaders. The medical practice act has possibly solved many problems, and the maintaining of high standards of medical practice is good, but the present trend of cooperation and sanction of ancillary persons dealing with the bodies and minds of sick persons will lead to decadence in the quality of medicine. Too many coexisting organizations and too many unqualified people have become private practitioners in the field of medicine. The unscientific and socialistic approach leads to physician deterioration and patient mortality while the scientific methods leads to beneficial results.

The solution to the problems of medicine will result only from unity, philosophic dedication, research, knowledge, understanding, sensitivity, and motivation. These attributes of a great physician will do much to stem the ever-mounting tides and sanctions of socialized medicine, state medicine, political medicine, third-party medicine, and profiteering medicine. Thus far, for the most part, the various forms of medical practices have been executed voluntarily by physicians. It is an error of judgment and lack of social perspective to cooperate with detrimental programs. A return to fundamental principles of scientific medicine and the practice of basic values is necessary if progressive medicine is to survive. There are many physicians who want to practice good medicine and who object to being sold into slavery for a few pieces of silver.

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THE STANDARD NOMENCLATURE AND THE INTERNATIONAL STATISTICAL CLASSIFICATION

To the Editor:—As Chairman of the Advisory Medical Board of the Standard Nomenclature of Diseases and Operations published by the American Medical Association, I am seriously concerned about the adverse effect which a report published in the June, 1959, issue of the *Journal of the American Association of Medical Record Librarians* may have on the future use of the Standard Nomenclature in hospitals.

Ten hospitals maintained dual indexes of diseases and operations in their record rooms, one using the numerical coding system of SNDO and the other, the coding system of the International Statistical Classification of Diseases, Injuries, and Causes of Death. The comparative trial is reported to have revealed that the coding and posting time was less with the ISC than with the SNDO. In using the two indexes to obtain records for study, it is reported that not only more records pertinent to the request but also more nonpertinent records were found in the ISC than in the SNDO indexes. These results could have been predicted, for a system with far fewer disease groupings will obviously take less coding and posting time than a more detailed and refined index. Also, the use of a simpler classification with more inclusive groupings will result in more pertinent and, also, more nonpertinent records being drawn from the files for study. In fact, if the experiment had included a consideration of some uncommon diseases, the use of the simpler system with coarse disease groupings would have resulted in drawing a predominant number of nonpertinent records from the clinical files.

Having participated as a member of the United States Committee on Health and Vital Statistics in the last two decennial revisions of the International List, I am aware that the ISC is intended primarily to facilitate the exchange of information on diseases, injuries, and causes of death for public health and administrative purposes. It was not designed for clinical research. If the ISC were to be expanded and its details multiplied to meet the special needs of clinical research, the relative saving in the coding and posting time, its chief advantage over the SNDO indexes, would be wiped out.

The authors of the report on the comparative study admit that almost all the medical record librarians who participated in the study "tend to prefer the greater specificity of SNDO." The authors assume that "this preference is probably affected by greater familiarity with one system than another," but this assumption is unwarranted for the participating medical record librarians expressed their preference after a full year's experience with ISC.

The authors of the report admit that "The SNDO, constructed by expert physicians, is the official nomenclature accepted in the US. The ISC is a classification system, not a nomenclature. . . . Physicians should not be given the ISC manuals to use as an aid in recording diagnoses since this would tend toward use of poor diagnostic terminology." Yet this is exactly what will happen in many hospitals if they abandon the use of SNDO in their record rooms and substitute the ISC indexes. Physicians will soon tend to forsake the use of SNDO, with resulting deterioration in the accuracy and completeness of diagnostic information.

It has taken more than 30 years to develop SNDO and achieve its employment by physicians in hospitals throughout the United States. During these years, it has taught many thousands of medical students, residents, and attending physicians to use exact and meaningful medical terms. The use of SNDO has simplified the work of record room librarians by enabling them to obtain complete diagnoses from the clinical services, which are ready for accurate filing in the disease and operation register.

The report fails to disclose any advantages of the ISC system of sufficient importance in hospital work to counterbalance the serious clinical and educational loss to American medicine which is bound to follow its introduction in hospital record rooms as replacement for SNDO. I sincerely hope that this will not happen.

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MISCELLANY

THIRD-PARTY MEDICINE—PAST, PRESENT, AND FUTURE

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Medical students have informed me that they hear and read virtually nothing which answers their growing curiosity about third-party practice as they approach their entrance into the private practice of medicine. My views on this subject were sought because I am engaged in the private practice of surgery and have also engaged in the encouragement and planning of third-party medical programs in our community.

The term "third party" appears in the 1955 edition of the American Medical Association's "Guiding Principles for Evaluating Management and Union Centers" which, among several features, quotes chapter 7, section 4, pages 26-27 of The Principles of Medical Ethics of the American Medical Association, December, 1954: "Free choice of physician is defined as that degree of freedom in choosing a physician which can be exercised under usual conditions of employment between patients and physicians. The interjection of a third party who has a valid interest, or who intervenes between the physician and the patient, does not per se cause a contract to be unethical. A third party has a valid interest when, by law or volition, the third party assumes legal responsibility and provides for the cost of medical care and indemnity for occupational disability." This statement, through which the American Medical Association approves as ethical properly conducted contract medicine, is apparently the origin of the expression "third party." While the expression is of recent origin, the practice is as ancient as medicine itself. We must, for the purposes of this dissertation, keep in mind that there is a difference between medical art and medical economics. The former is the collection of techniques and skills employed in the prevention and treatment of diseases. The economics comprehends the usages, conditions, and arrangements under which medical services are available.

Little doubt exists that progress in medicine could not have flourished as it has without the aid of third parties. Every culture, however primitive or advanced, has been confronted with a number of basic needs of its people for food, clothing, shelter, a common defense, a moral code, and a variety of entertainments to escape from the humdrum routine of life. Among the mightiest of these great tasks is the maintenance of the health of the people. The success of this effort depends not only on medical technology but also on the economic arrangements under which the medical arts are dispensed.

Historical Evolution

Third-party medicine was one of the great forward steps in civilization. From the earliest days the king had his personal physician, and the latter attended to the physical needs of the entire court, although he was paid and maintained by the king. Even earlier than that, the first manifestation of the good neighbor was found in the story told by the Lord of the unfortunate man who fell among thieves on the road from Jerusalem to Jericho. The Good Samaritan bandaged up his wounds, took him to the inn, and left money for his care, perhaps the first record of third-party medicine.

In his historical evolution man discovered what he called freedom and he harkened back to the days of Athens and Sparta and began to form republics. Even the legislators and tax collectors derived their position and income from the taxes paid by people whom they served, but whom they never saw or knew. Industry also learned that the most efficient way to transact big business was through corporations, although this device, even as far back as Ancient Greece, had never been used except for such things as the maintenance of universities. In the United States, it was not until after our Civil War that the corporation was applied to big business, and this became the birth of the most serious third-party activity of all times.

Until about 1890, a laborer earned about one dollar a day. A man named Samuel Gompers organized workers on the basis that everyone was entitled to fair compensation for his toil and to some enjoyment in life. He organized labor on a fair and just basis, so that the man who worked conscientiously had the kind of opportunity which was taken advantage of by many of our men who subsequently rose from rags to riches. Nowhere in history have so many received so much through opportunity and returned so much to others in labor as in the United States. In the provision of opportunity and improved working conditions, however, medical care and maintenance of health became significant factors.

Hospitals first came into existence along the battlefields of the Holy Land during the first crusade, provided and maintained by a benevolent third party known as the Knights of St. John, who subsequently became the Knights of the Cross and whose chief later became the first king of Prussia. It was found in our early experience with hospitals in the United States that people coming to them could not pay. Hospitals depended for financing on endowments and charitable contributions which, however, were sporadic; thus hospitals could not maintain themselves.

Development in the United States

Until about 1880, life insurance was looked on as immoral, since many contended that it put a premium on murder. Yet today no head of a family in even the humblest circumstances would think of

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Annual Phi Rho Sigma Lecture, St. Louis University Medical School, March 3, 1959.

leaving his family unprotected by life insurance. As insurance theory and practice grew and prevailed, not only for life but for protection against unusual losses by fire, theft, and accident, it became logical that the successes in these operations should be applied to protection against losses by sickness and injury. As society grew more complex it was found that, where a serious sickness arose, a family was set back as much as a year's earnings. Thus it was that the modern third party was introduced into medical care, and there has evolved active insurance company participation, including the nonprofit, "Blue" third-party programs of the medical societies. Doctor and hospital care could not exist as we know them today without the third party.

How active has this third party become in private medical care? During the 1929 depression few hospitals survived financially. Today it is likely that most private hospitals would be in desperate condition were it not for the effect of these third-party contributors. In our own Barnes Hospital (which may be typical of a medical center private hospital), 50% of dollar income is paid by third parties, approximately two-thirds of all patients' income is paid by third parties, and approximately two-thirds of all patients admitted to the hospital are sponsored by third-party contributors (personal communication from Dr. Crawford Vermillon, assistant director, Barnes Hospital). It is difficult to believe that any doctor very actively engaged in any type of private medical care today can honestly disclaim interest and participation in third-party medicine, which has been defined, both by official medical circles and by experience in this and other American communities, as ethical, legal, necessary, and prevalent. This should never be confused with socialized (government) medicine, which it strives, by the very nature of its voluntary aid, to oppose. It has become a popular subject in medicine during the past several years because of the great interest shown by the population in seeking access to modern medical care on a prepaid basis, as well as the increased third-party activity by industrial concerns, labor unions, and insurance companies representing large groups of individuals.

The oldest management third-party program dates back to 1868. The oldest union third-party program dates back to 1913, with approximately 50 such centers in operation today and, as pointed out by Dr. Robert Bassett at his recent installation as president of the St. Louis Medical Society, "Third Parties include: 1) Blue plans sponsored by doctors; 2) Commercial insurance companies; 3) Government agencies which control the Vendor program, Medicare, V. A., and other programs; 4) So-called independent plans; 5) Industrial medicine in all of its phases; 6) The widespread Labor Health plans, all to the extent that today over one hundred and ten million Americans have some protection against illness and accident (Bulletin, St. Louis Medicine, Jan. 14, 1959)."

In St. Louis, third parties of various types have long practiced employment of physicians for various degrees of medical service in behalf of their members. The following well-known and well-established industrial organizations practice third-party medicine: General Electric Company, Union Electric Company, United States Defense Corporation, Anheuser-Busch Company, Fisher Body Company, American Brake Shoe Company, Southwestern Bell Telephone Company, Emerson Electric Company, Mallinckrodt Company, Monsanto Chemical Company, International Shoe Company, Pevely Dairy Company, National Lead Company, General Cable Corporation, Famous Barr Company, McDonald Aircraft Company, Aeronautical Chart & Information Center, Frisco Railway, St. Louis Public Service Company, and numerous others. In addition, groups not to be classified as industrial or business concerns engage in the same type of third-party employment of physicians; and these include both St. Louis University and Washington University with their student health centers and medical schools, which provides employment for teaching and medical practice; family agencies and children's institutions; nursing homes; the St. Louis Society for Crippled Children; the city and county health departments; the city, county, and state hospitals; and others. Still another group performing as a third party in employing physicians in this community is organized labor through such plans as the Labor Health Institute of the Teamsters, the Medical Institute of the Meat Cutters, the Ladies Garment Workers Medical Center, the United Mine Workers program, and the Missouri Pacific Hospital Association.

Thus it is seen that the experience of medical practice with third-party agents is extensive in both duration and quantity in our own community, and there have been few doctors who have entered practice in recent years who have not engaged almost from the outset in some form of third-party practice, generally on a part-time basis. Local medical societies, as well as the American Medical Association Council on Medical Service, have achieved much during the past 15 years in encouraging and cooperating with insurance companies and service plans serving the best interests of their members. The underlying view is that there must be a common ground for providing voluntary medical insurance and service at reasonable rates to all Americans, especially those in the middle and lower income brackets.

Problems of Policy and Control

The appearance on the scene of a third party who will pay bills does not provide a complete solution to the problem. The American medical profession in very recent years made its position clear on this subject when it opposed the Murray-Wagner-Dingell bill, which sponsored socialized medicine with its offer to pay the bills. The medical profession made an emphatic reply of opposition to any attempt to federalize the practice of medicine in this country, as has been done in numerous other countries to the discredit and eventual deterioration of their medical standards. The medical profession now eyes the union third party not only with respect for what good it may accomplish in the health field by paying the bills of doctors, and hospitals, and others but also with alarm for what damage it may do to the standard of medicine if it attempts and succeeds, for reasons of self-aggrandizement or exploitation for power, in interfering with the first and second parties and the quality of the medical care extended. Some alarm results in part from the general unpopularity of labor unions and in part from the alterations in the traditional private patient-doctor practice. Doctors who have fancied themselves as rugged individualists and those who are neighborhood practitioners have seen their private patients disappearing to V. A. hospitals, industrial health centers, labor health centers, and elsewhere increasingly and are inclined, therefore, to oppose all plans as amounting to interference. Furthermore, there are those who are just as alarmed at the ultimate possibility of having powerful labor organizations or insurance companies dictate medical policy and medical financing as they were alarmed at the prospect of having the federal government dictate in this capacity.

To evaluate this labor third party, the Commission on Medical Care Plans of the American Medical Association has conducted several important surveys, including one with detailed descriptions of 29 union health centers that was reported in September, 1958. In their conclusions, the commission emphasized the generally high quality of medical care provided in the modern union health centers as compared to the standard of practice elsewhere in the United States.

What, then, becomes the future trend in third-party practice based on past and present experience and, specifically, what are the answers for those now completing their medical training and about to embark into this socioeconomic whirl of first, second, and third parties?

Would that I could borrow the wisdom and ability of the divinely inspired Moses, or Polonius, or the elder Germont. But, alas! I feel no security in predicting what is best. There are, however, some self-evident facts on which one can safely proceed.

Medical technology has improved immensely, and medical economics is changing in response to the greatest challenge of our time, viz., how to make this high quality of medicine obtainable by all. In this medico-economic reformation, the physician should be vigilantly responsible for opposing any change which will threaten to sacrifice the quality of medical achievement or its continued progress. He must also be mindful of all people's demand for this care and cooperate in planning with them and their third-party representatives how to make it available to them at reasonable cost.

False issues between physicians must be recognized and eliminated. The various techniques of medical practice today (solo, group, general, specialist) are all well-established, ethical, and legal and all are competent to provide excellent medical care. "Fee-for-service," "prepaid care," "salary contracts," and "third party" per se are all ethical and acceptable to organized medicine. It is not likely or necessary that any one system of practice will ever serve the various interests among the purchasers of medical care, and there is no place for competitive tensions between such participants.

Socialized (government) medicine must be opposed, although federal, state, and local governments are now widely engaged in medicine in the United States. Wherever voluntary groups and private enterprise can be encouraged to do the work, they deserve the cooperation and aid of doctors, since it is historically established that government domination of medicine leads to an inferior quality which Americans need not and have not settled for.

Recommendations

In my own experience and deliberations on the subject, I have concluded that the extraordinary achievement in the standard and quality of medical practice in the United States must be protected by regulation, so that it does not get lost in the many changes and influences to which it is being, and will be, subjected by the economy. This protection must be provided by those who have developed and practiced this quality, the doctors. I believe it is urgent that the American Medical Association recommend that any physician who accepts employment by a third party in caring for patients should have in his possession a contract which guarantees protection of the ethics of the profession and the delegation of medical policy and quality to the doctors. The American Medical Association should provide a type of contract for this purpose and it should include the following points: (1) assurance that the third party will not interfere in strictly medical matters dealing with traditional doctor-patient relationships; (2) assurance that professional qualifications for participating personnel be determined entirely by the profession, without lay interference; and (3) assurance that any disputes between medical and lay members will be settled through joint negotiations and then, if necessary, by impartial arbitration.

If the practice of third-party medicine will ultimately result in the domination and control by a business head, then such a practice would be not only unethical but also uneconomical and immoral. The only way to prevent such an undesirable result is for organized medicine to appreciate the impending danger and to take necessary steps, nationally and locally, to prevent the catastrophe. Will the future of medical practice be dominated by the business head of third-party organizations or by the guardians of the ethics of our profession?

THE LEISURE CORNER

THE RING COLLECTOR

The small band known to us as the finger ring has been an ornament and an expression of affection for thousands of years. The custom of wearing rings is probably as old as man. Rings have been found in ancient Egyptian tombs. They have long been symbols of a ruler's authority; kings gave their rings to trusted servants, and the ring gave the wearer the power of king's messenger. The Bible relates that Pharaoh placed his signet ring on Joseph's finger and that from this ring all men knew that Joseph had the sovereign powers of a king. The Romans probably originated the use of engagement or betrothal and wedding rings, a custom continued throughout the world to the present day.

Superstition surrounds the earliest legends concerning rings. Many people still tie strings around their fingers as a reminder. This tradition goes back to Mount Olympus, where Prometheus was said to have been chained for 1,000 years because he dared steal the sacred fire of heaven for mortal use. Jupiter took pity on Prometheus and bade him go free, with the proviso that he wear part of the chain around his finger, a reminder of his past servitude.

Primitive men would tie bands of sweet grass or narrow thongs of leather about the fingers of their women to remind them to remain faithful while they were away hunting game. Today, wedding rings are presumed to remind men and women that they are married. Rings are also worn to commemorate birthdays, school graduations, friendships, and memberships in organizations. Most rings are made of gold or other precious metals, plain, engraved, or set with stones. The most popular precious stone used in ring settings is the diamond, but others widely used are amethyst, topaz, turquoise, emerald, pearl, ruby, and sapphire.

Since human beings fear illness and death most, it can come as no surprise that throughout history rings have been worn to combat the possibility of the "evil eye," demons, witches, illness, and weakness, in fact every type of danger and disease. In warding off devils, madness, and death rings have long been regarded as possessing unusual curative and preventative powers. This was particularly true in the case of "cramp" rings. The fear of cramps was at one time as acute as the fear expressed by some swimmers today; the spasmodic and powerful contraction of the muscles was thought to produce permanent paralysis. But if a ring blessed by holy men were worn, it would ease the discomforts that ensued.

The collecting of rings and the study of their historical background has provided a fascinating hobby for many doctors because the association with disease has made the ring a symbol both therapeutic and psychological. Rings made of silver were once worn to cure fits and convulsions, rings made of elk hoof to cure epilepsy. Rings made of pure silver "of the moon," set in a piece of elk hoof under proper zodiacal signs and during the favorable conjunction of the planets, would prove "certain" to cure all diseases of the brain. Nasal congestion was treated by inserting medicated rings in the nostrils of patients.

Galen, who gained great fame as a general practitioner in Rome early in the 2nd century, wrote about a ring set with sard (a variety of cornelian) which weighed 20 grains and was supposed to insure deep and tranquil sleep and give protection against troublesome dreams and fearsome visions. Marcellus Empiricus, who practiced medicine in the 6th century, recommended a finger ring made of the hoof of a rhinoceros. He claimed that any patient suffering from "obstruction of the nerves" would experience relief by wearing the ring. Rings were also used as antidotes against poison. One example concerns a toadstone set in an open ring that would produce, it was claimed, a sensation of heat at the point of contact with the skin. Rings were also prescribed for respiratory tract disorders, notably sneezing and coughing. Infection, on the other hand, was treated by rubbing a gold ring firmly against the infected area, which would supposedly draw out the pus and alleviate the infection. Bilious and intestinal difficulties were not overlooked; a 6th century medical practitioner named Alexander Trallianus prescribed a type of ring that was proclaimed to cure kidney disorders, ulcers, and leprosy.

During the 16th century rings were worn on specific fingers in keeping with the occupation or personal inclination of the wearer. Thus, doctors wore rings on the thumb, merchants on the index finger, jesters on the middle finger, students (not lovers) on the annular finger, and lovers on the auricular (small) finger.

Ring collectors are constantly looking for interesting inscriptions to convey the sentiments of the giver of a ring. The following inscriptions were found at random in various books dealing with rings:

My giving this
Begins thy bliss.

Hearts content
Can ne'er repent.

And as this round is nowhere found
To flaw, or else to sever,
So let our love as endless prove,
And pure as gold forever.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Some Observations on the Malabsorption Syndrome, Based on the Use of Absorption Tests and Biopsy of the Small Intestine. P. J. Culver, J. A. Benson Jr., E. Strauss and C. M. Jones. Gastroenterology 36:459-466 (April) 1959 [Baltimore].

Since surgical exploration for biopsy of the small intestine is too formidable a procedure for the study of most patients with the sprue syndrome, the announcement by Shiner of a practical peroral biopsy tube is welcome news. Tools are now available for correlating the histology of promptly fixed specimens of intestinal mucosa with the absorptive functions of the small intestine. It was the aim of the studies described to compare the histology of "freshly fixed" surgical biopsy specimens of the small intestine with specimens taken via the Shiner tube from the same area, and in one case with postmortem material. Laparotomy was performed on 7 patients admitted with a diagnosis of sprue. Biopsies of a segment of the upper jejunum were performed without the application of clamps. In 3 patients the Shiner tube was passed just prior to the surgical biopsy, and a specimen was taken from the same area of the jejunum. The specimens were immediately fixed in 10% formalin in the operating room. One patient died of acute coronary thrombosis on the 11th day after laparotomy, providing material to show the changes of postmortem autolysis. An 8th patient with long-standing sprue did not have a laparotomy, but formalin was injected into the stomach and abdominal cavity immediately after death. The tissues were routinely blocked in paraffin, and sections were stained with hematoxylin and eosin. The histological studies on the intestinal specimens focused attention on the thickness of the mucosa (atrophy); aspects of the villi; arrangement, size, shape, and cytoplasm of the epithelial cells, and also various aspects of the nuclei of these cells; the lamina propria; and the submucosa.

In order to arrive at an approximation of the severity of morphologic change, the findings which might alter surface area, activity of the villi, epithelial cell function, and transport of foodstuffs away from the intestinal mucosa were evaluated. Then a composite estimate of the over-all histological defect was made. Results of the various biochemical tests for measuring intestinal absorptive function in each patient were likewise pooled to provide a composite estimate of the degree of malabsorption at the time of biopsy. All the patients studied had histological abnormalities of the small intestine, but the abnormalities found have not yet been demonstrated to be specific for sprue. There was dissociation between the severity of histological abnormality and the severity of malabsorption. This suggests that biochemical abnormalities of the intestinal mucosal cells may be the primary factor in the pathogenesis of the sprue syndrome.

Clinical and Pathological Studies of Joint Involvement in Sarcoidosis. L. Sokoloff and J. J. Bunim. New England J. Med. 260:841-847 (April 23) 1959 [Boston].

The authors report on 5 negro patients, a 33-year-old man, 3 women between the ages of 24 and 33 years, and an 11-year-old girl, with sarcoidosis in whom polyarthritis was a conspicuous feature. In 3 patients, arthritis was the initial or early manifestation of sarcoidosis. In each of the patients, systems other than the joints were involved in the sarcoidosis; 2 patients had sarcoid of the skin, 1 had erythema nodosum, 2 had uveitis and other ocular lesions, 4 had pulmonary involvement, and 4 had hilar adenopathy. Biopsy established the presence of noncaseating tubercles in the synovial tissue in 3 patients, and a submiliary granuloma suggestive of sarcoid in a 4th patient. In the 5th patient, the synovitis was of nonspecific histological nature. No fungi or acid-fast organisms could be recovered from the lesions. Although bone lesions were present in 3 of the 5 patients, the phalanges of the hands being affected in 2 and the phalanges of the feet in 1, the joint disease was not secondary to that in the bone and must be regarded as an intrinsic manifestation of the sarcoidosis. There is reason to believe that joint involvement of this sort is commoner than has been recognized previously, and that it has been mistakenly diagnosed as rheumatic fever or rheumatoid arthritis. Although erythema nodosum was present

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The place of publication of the periodicals appears in brackets preceding each abstract.

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in only 1 of the 5 patients, it has been present in most of the cases reported by other workers. The frequency with which the lesion is associated with erythema nodosum invites speculation about the role of hypersensitivity in the pathogenesis of the disorder and also raises the question whether the arthritis and adenopathy of erythema nodosum are not themselves inherently related to sarcoidosis. Synovial biopsy may be of diagnostic value in such cases.

Agammaglobulinemia: Report of a Case of Historical Interest. H. B. Slavin, E. L. Alling and E. H. Keutmann. New England J. Med. 260:852-856 (April 23) 1959 [Boston].

The authors report the case of a male patient who was 13 years old when first seen in 1927 in the pediatric outpatient department of the Strong Memorial Hospital in Rochester, N. Y. He was underweight, complained of lassitude, and had had many sore throats. In 1933 he was seen at the Rochester General Hospital because of persistent, productive cough. He had left-side basilar bronchiectasis. A phrenicectomy was performed in 1934. In 1936 he was again admitted to the hospital, at this time for pneumonia. In 1937 a myringotomy was done for otitis media. From October, 1939, until his death in September, 1942, at the age of 29 years, he was hospitalized for 465 days, during 353 of which he had fever associated with cellulitis of the right thigh, antral sinusitis, acute proctitis, pneumonia, erythema nodosum, generalized arthralgia, a peritonsillar abscess, otitis media, appendicitis, bronchopneumonia, and parotitis. In November, 1941, he was found to have hypoglobulinemia. This was the first time that the plasma protein levels were determined. The electrophoresis apparatus was not available for study of the patient's plasma proteins until April, 1942. The electrophoretic analysis revealed a complete absence of the gamma peak.

The effect of hyperimmunization with horse serum, the patient's sensitivity to tuberculin and sulfathiazole, absence from the circulation of antibodies against a bacterium that caused repeated infection (type 19 pneumococcus), and failure to detect hemolytic complement in the blood serum, together with marked proliferation of the reticulum of lymph nodes and absence of plasma cells from all the tissues examined, are described and discussed. After a transfusion of normal plasma, gamma globulin did not appear to be removed from the blood stream faster than normal. The absence of a history of recurrent bacterial infections in infancy or early childhood and of detectable bacteremia during the frequent occurrence of such attacks in later life, together with the fact that the patient lived for 29 years, suggests that this case of agammaglobulinemia was the so-called acquired type.

Study on the Behavior of Bromsulphalein in Jaundice Diseases. I. Oddone, G. C. Bruno and P. C. Micheletti. Minerva med. 50:781-788 (March 17) 1959 (In Italian) [Turin, Italy].

The behavior of Bromsulphalein in 34 patients with different jaundice affections was studied. Eight patients had posthepatic (or obstructive) jaundice with no evident signs of hepatic damage, 5 had posthepatic jaundice with evident signs of hepatic damage, 5 had acute hepatitis, 3 had hepatocholangeitis, 11 had cirrhosis, and 2 had prehepatic jaundice. Bromsulphalein retention tests made in all the patients 30 minutes after the injection gave uniform results; the highest retention value (74%) was obtained in a patient with obstructive jaundice and no apparent hepatic damage, and the lowest value (16%) in a patient with acute hepatitis. Retention tests made 24 hours after the injection of Bromsulphalein yielded the highest values in patients with posthepatic icterus; values obtained in patients with hepatic damage were lower than those in patients with no damage. The lowest retention values were obtained in patients with cirrhosis. Intermediate values were obtained in patients with hepatitis. Values obtained in patients with hepatocholangeitis were similar to those obtained in patients with obstructive jaundice. Tests to determine the values of the constant of Bromsulphalein fall in the blood gave the lowest values in patients with posthepatic jaundice and no apparent damage; values increased markedly in patients with posthepatic jaundice and evident liver damage; the highest values were obtained in patients with cirrhosis. Intermediate values were obtained in patients with hepatitis and in those with hepatocholangeitis. Tests to determine the percentage of Bromsulphalein eliminated through the bile ducts yielded the highest values in patients with cirrhosis and in those with hepatitis. Values obtained for the remaining patients were high in those with jaundice with evident hepatic damage and low in those with no damage. The results obtained with tests to determine the period of persistence of Bromsulphalein in the blood and the quantity of coloring substance eliminated in the first 24 hours through the emunctory action of the kidney were comparable to those obtained with retention tests 24 hours after the injection of the drug.

Cirrhosis in Women: A Clinicopathologic Study. L. G. Stuhler, A. H. Baggenstoss and H. R. Butt. Gastroenterology 36:467-479 (April) 1959 [Baltimore].

The authors point out that de Josselin de Jong in 1931 defined cirrhosis on the basis of 3 common pathological characteristics: (1) degeneration and death of hepatic cells, (2) proliferation of connective tissue, and (3) regeneration of hepatic cells. These 3 criteria have been the subject of intensive investigation. Although some investigators have placed great emphasis on the connective tissue reaction, the authors have stressed the role of the regeneration of the hepatic cells, particularly in the form of the regenerative nodule, as the important physiopathological condition in cirrhosis after destruction of the parenchyma. Accordingly, they have accepted as examples of cirrhosis in women only those instances in which nodular regeneration was a feature of the reparative process. The natural history of some diseases is different according to the sex of the person afflicted. This study is concerned with cirrhosis as it affects women.

The material for this study included all cases in which cirrhosis of the liver in women, as defined above (except cirrhosis associated with obstruction of the biliary tract, congestive heart failure, hemochromatosis, or hyperthyroidism), was studied on autopsy at the Mayo Clinic during the years from 1924 to 1954, inclusive. There were 86 women with cirrhosis among a total of 5,515 women subjected to autopsy. The commonest type of cirrhosis found was the postnecrotic type (73 of 86 cases). The commonest cause of this type of cirrhosis was viral hepatitis (either infectious hepatitis or serum hepatitis). Cirrhosis in women, and particularly postnecrotic cirrhosis, was present at an earlier age than in men (average age, 45 years). Laennec's cirrhosis was found in women who were a decade or so older than the aforementioned women (average age, 55 years). Viral hepatitis in women may produce a granular type of cirrhosis, which bears some superficial resemblance to Laennec's cirrhosis but which can, in most instances, be distinguished histologically from typical Laennec's cirrhosis. Alcoholism is the etiological factor most commonly found in Laennec's cirrhosis in women, as it is in men.

The time interval between the onset of hepatitis and the development of cirrhosis was as short as 9 weeks and as long as 20 or more years, but in the majority of cases studied cirrhosis developed within a 3-year period after hepatitis had been contracted. The development of edema and ascites in both types of cirrhosis and of jaundice in Laennec's cirrhosis generally indicated a poor prognosis. Laennec's cirrhosis in women, as in men, appeared to be most often a progressive disease of several years' duration. This type of cirrhosis was much more likely to be a subclinical pathological finding than was the postnecrotic or granular posthepatitis type of cirrhosis. Postnecrotic cirrhosis generally had a more rapid clinical course, with death ensuing within a shorter period after the liver had been injured. The clinical manifestations usually were more pronounced in this type. Thus, the incidence of latent cirrhosis of this type, as found at autopsy, was considerably less than that of Laennec's cirrhosis.

Peculiarities in the Course of Malignant Diseases of the Hematopoietic and Lymphoreticular Systems Under Treatment with Cytostatic Drugs. W. Siegenthaler, G. Keiser and H. U. Zollinger. Ztschr. klin. Med. **155**:568-601 (no. 6) 1959 (In German) [Berlin].

The authors attempted to ascertain whether, since the introduction of cytostatic drugs into the treatment of malignant diseases of the hematopoietic and lymphoreticular systems, changes have taken place in the clinical aspects of these diseases. They compared observations on 120 patients with these disorders, who were treated at clinics and hospitals in Zurich, Switzerland, during the years 1954-1957 when cytostatic drugs were used or were combined with roentgen irradiation, with those on an equal number of patients treated between 1947 and 1953 when cytostatic drugs were not used or were used only briefly and in not very potent forms. The fact that in the 4-year period ending in 1957 the same number of patients with these malignant diseases were treated as in the preceding 7-year period suggests increasing frequency, and this was the case with regard to the percentage of total admissions (from 0.6% to 1%). This increase, however, may be largely due to the fact that, with the availability of more and presumably better modes of treatment, practitioners refer more patients with these malignant diseases to the special clinics.

The 120 patients treated more recently included 29 with acute leukemia, 9 with chronic myeloid leukemia, 19 with chronic lymphatic leukemia, 23 with sarcoma of the lymphoreticular system, 10 with multiple myeloma, and 30 with Hodgkin's disease. Thus, there were 57 patients with malignant conditions of the hematopoietic system and 63 of the lymphoreticular system. The incidence during the preceding 7 years was largely the same, that is, there were 65 patients with malignancies of the hematopoietic system and 55 of the lymphoreticular system.

In comparing the 2 groups, it was found that under the influence of the cytostatic drugs the survival of patients increased, especially those with acute leukemia for whom mercaptopurine (Purinethol) was the cytostatic drug most often used. In chronic lymphatic leukemia triethylenemelamine (TEM) and, more recently, chlorambucil (Leukeran) were used. Nitrogen mustard was widely used in patients with malignancies of the lymphoreticular system and in those with Hodgkin's disease. In general, the number of patients with each type of disease was not large enough to arrive at a definite conclusion with regard to changes in the prognosis under the influence of the cytostatic drugs. These drugs did, however, produce some changes in the clinical course. Most noteworthy was the increase in serious complications, such as damage to the bone marrow, severe infections, embolisms, and others. The fact that 41% of the patients treated with cytostatic drugs died, not of malignant processes in the hematopoietic and lymphoreticular systems, but of other causes deserves serious consideration. While knowledge of these complications should not prevent further employment of the cytostatics, antibiotics and cortical hormones, which are suitable prophylactics, should be given, so that the potent cytostatics will not produce undesirable secondary effects.

Bone Marrow Embolism to Lung Following Sternal Puncture. J. H. Yoell. A. M. A. Arch. Path. 67:373-374 (April) 1959 [Chicago].

Red marrow emboli to the lungs have been known to occur in fatal cases of multiple fractures, but there has been only a single literature report showing that these emboli may also arise as the result of sternal puncture. The patient cited by Montgomery in 1951 died 6 hours after such a puncture. The author describes a second case, that of a 70-year-old man with a long-standing history of chronic pyelonephritis and renal failure. Autopsy confirmed the clinical diagnosis. An incidental microscopic finding consisted of a single, solidly lodged, red marrow embolus within a small pulmonary vessel. Clinical records disclosed that sternal puncture and aspiration biopsy with a Turkel needle had been performed 9 days before death.

Marrow embolism subsequent to sternal puncture is no longer merely theoretical. Such emboli may be bland and few (present case) or fatal and multiple (Montgomery's experience). Reported instances of red marrow embolism, judged to be the immediate cause of death, have been encountered with neoplastic and tuberculous pathological fractures of vertebrae and after thoracotomy. A somewhat different mechanism, namely, bone marrow infarction, has led to fatal red marrow embolism in a few cases of sickle-cell anemia and type C hemoglobin disease. Red marrow embolism to the lungs incident to needle aspiration of a marrow space adds another, although so far rare, risk to this common diagnostic procedure.

Cardiovascular Lesions of Scleroderma. A. Buzzi, A. Bertolotto, G. Buzzi and L. Yraola. Prensa méd. argent. 45:3281-3287 (Oct. 10) 1958 (In Spanish) [Buenos Aires].

A 61-year-old woman with diffuse scleroderma and vascular disorders of the type of Raynaud's phenomenon of 30 years' duration is reported on. Severe skin lesions occupied the forearms up to the upper third and the legs up to the middle third. The middle finger of the right hand had been amputated 2 years before consultation because it became gangrenous. On hospitalization, the patient had massive gangrene of the left hand and its 5 fingers and of the toes and borders of the right foot. Roentgen-ray examination of the chest showed prominence of the aorta and of the root of the pulmonary artery; similar examination of the hands, arms, and legs showed calcinosis of the fingers, elbow, and knee joints. The calcium metabolism was normal. The electrocardiographic changes corresponded to those of ventricular hypertrophy and necrosis of the lower surface of the myocardium. An anatomicopathological examination of the hand, surgically removed, showed thrombosis of the digital arteries and lymphocytic and monocytic infiltration and edema of the arterial walls of the palmar arteries.

Diffuse scleroderma is a visceral disease which develops in association with arthropathy and skin lesions. The disease involves mainly the lungs and the cardiovascular system. Peripheral vascular disorders of the type of Raynaud's phenomenon are typical and constant; they appear early in the course of scleroderma. Electrocardiographic changes showing either overload or hypertrophy of the right ventricle are frequent. The ventricular abnormality is due to hypertension of the pulmonary artery. The extent of the electrocardiographic changes depends on the severity of the cardiovascular disorders.

Radioactive Phosphorus in the Treatment of Chronic Leukemias: Long-Term Results Over a Period of 15 Years. E. H. Reinhard, C. L. Neely and D. M. Samples. Ann. Int. Med. 50:942-958 (April) 1959 [Lancaster, Pa.].

From January, 1942, until busulfan (Myleran) came into use in 1953, practically all patients with chronic granulocytic leukemia referred to the hematology division of Washington University school of medicine for therapy were given radiophosphorus (P^{32}) as the primary treatment. Similarly, from January, 1942, until 1955, when chlorambucil (Leukeran) came into use, most of the patients with chronic lymphocytic leukemia were treated with P^{32}. Subsequent to 1953 and 1955, a progressively larger percentage of the patients with chronic granulocytic leukemia and chronic lymphocytic leukemia, respectively, were treated with Myleran and Leukeran. Data are presented concerning the results of therapy in 102 patients with chronic lymphocytic leukemia and in 118 patients with chronic granulocytic leukemia who were treated predominantly with P^{32}.

Forty-five per cent of the patients with chronic lymphocytic leukemia and 57% of the patients with chronic granulocytic leukemia showed a marked decrease in the size of enlarged lymph nodes during or immediately after the initial course of P^{32} treatment. The effects of the initial course of this therapy on spleen and liver enlargement have been presented graphically in such a manner as to simplify the comparison with the comparable effects of chemotherapeutic agents. If the leukocyte level was elevated at the time P^{32} therapy was started, a substantial decrease in the white blood cell count occurred in practically all cases. Of 57 patients with chronic granulocytic leukemia who had an initial thrombocyte count of one million per cubic millimeter, the platelet count decreased significantly after treatment in 22. Only 2 out of 23 anemic, nontransfused patients who had chronic lymphocytic leukemia showed an increase of 2 Gm. or more in the hemoglobin level after P^{32} therapy, whereas 22 out of 46 anemic, nontransfused patients who had chronic granulocytic leukemia had such an increase in the hemoglobin level. No patient with chronic lymphocytic leukemia who had an initial significant thrombocytopenia experienced an increase of the platelet level to normal after therapy, whereas such an increase occurred in 2 of the 8 patients with chronic granulocytic leukemia who had thrombocytopenia at the time P^{32} therapy was begun. The 5-year survival was 51% in patients with chronic lymphocytic leukemia and 12.5% in those with chronic granulocytic leukemia.

Segmental Ulcerative Colitis—Classification: Report of Nine Unusual Cases. E. J. Kurt and C. H. Brown. Am. J. Gastroenterol. 31:419-431 (April) 1959 [New York].

Segmental ulcerative colitis has been defined to include only that type of colitis that is limited to a segment or a portion of the colon, with no involvement of the terminal ileum or the rectum. Of 1,150 patients with ulcerative colitis seen at the Cleveland Clinic between 1940 and 1958, only 9 had true segmental ulcerative colitis. Cases in which involvement of the terminal ileum was questionable were excluded. The average period of follow-up was 5 years and 9 months. Medical treatment was given initially to 7 of the 9 patients. The condition of 4 patients improved satisfactorily, while in 3 the disease progressed and surgery was required. Of the 9 patients, 5 underwent surgery. Good results were achieved in all of them, although some patients required more than one operation. Two of the 3 patients on whom segmental resections of the involved areas were performed had no recurrence of colitis within 4 and 5 years.

The authors believe that segmental ulcerative colitis should be treated in much the same way as the commoner chronic ulcerative colitis is treated. Intensive and continuous medical management should be given adequate trial before surgical intervention is considered. Because of the bizarre involvement of the colon, all patients with segmental colitis should have several warm-stool examinations. A thorough course of antiamebic therapy is indicated even when the findings are negative. If adequate medical treatment fails to effect a remission, surgical intervention is indicated. Surgical treatment should remove completely the diseased tissue, but at the first operation preservation of normal intestine (i. e., segmental resection) is advisable. If there is incapacitating recurrence, subtotal colectomy with ileoproctostomy or total colectomy with end-ileostomy may be performed subsequently.

Flare-Up of Pericarditis Complicating Myocardial Infarction After Two Years of Steroid Therapy. W. Dressler. Am. Heart J. 57:501-506 (April) 1959 [St. Louis].

Pericarditis may occur as a complication of myocardial infarction and is then often associated with pleurisy and pneumonitis. The condition has been referred to as postmyocardial infarction syndrome. It has a characteristic tendency to recurrences, resembling in this as in other respects the postcommissurotomy syndrome. Both conditions are dramatically relieved by corticosteroids. Withdrawal of hormones is usually followed by a mild rebound. In occasional instances, however, the flare-up is severe and may occur repeatedly after months or even years of steroid therapy. In the 58-year-old man whose case is described, a remarkable sequence of events followed acute myocardial infarction. The initial febrile period was prolonged and was characterized by pleuropericardial pain and hemorrhagic expectoration. Pulmonary infarction was thought to be the cause. However, fever and chest pain of pleuropericardial type relapsed for 8 weeks, while hemorrhagic sputum was no longer present. Nor did the electrocardiogram reveal evidence of an extending myocardial lesion. The diagnosis was then changed to recurrent pneumonia. Numerous antibiotics failed to influence the febrile course. In the 8th week of illness, when the chest film indicated enlargement of the heart silhouette in addition to pleurisy, a postmyocardial infarction syndrome was diagnosed; steroid therapy was instituted and relieved all manifestations of the illness. However, repeated attempts at withdrawal of the hormones resulted in flare-ups of fever and chest pain. On 2 occasions, that is, 10 months and 2 years, respectively, after onset of steroid therapy, discontinuance of hormone administration produced symptoms and signs of pericardial effusion, pleuritis, and pneumonitis.

The observations on this patient represent another argument against the view that the postmyocardial infarction syndrome is of infectious origin. The author observed similar severe and recurrent withdrawal reactions in 2 other cases of postmyocardial infarction syndrome, in one of which signs of adrenal insufficiency developed, necessitating continuation of hormone therapy for a prolonged period of time. These drawbacks have to be borne in mind when the question of the use of hormones arises. Some patients with postmyocardial infarction syndrome do not require steroids, because the complication may subside spontaneously after a short time. Hormone therapy should be reserved for severe cases with prolonged course and intractable pain.

The Frequent Association of Other Body Tumors with Familial Polyposis. D. C. Collins. Am. J. Gastroenterol. 31:376-381 (April) 1959 [New York].

Fourteen new instances of an association between various secondary hard and soft tissue tumors and proved congenital polyposis are added to the literature. Twenty-nine other examples of an association of this familial colonic disease with other abnormal growths have been recorded during the past 20 years. Physicians are urged to remember the frequent association of these 2 pathological entities and to rule out, at the earliest possible moment, the possible presence in patients of an unsuspected instance of precancerous familial polyposis. Under such circumstances, if 2 specific diagnostic tests are performed (proctosigmoidoscopy and barium enema), many additional lives will be saved from needless death through the inevitable future development of carcinoma of the large intestine.

The Ion-Exchange Method of Determining Gastric Acidity. D. C. Mortimer. Canad. M. A. J. 80: 607-609 (April 15) 1959 [Toronto].

The author used Diagnex blue, a carbacrylic cation exchange resin, in which the hydrogen ions of the resin have been exchanged with azure A ions, a dye indicator, for the detection of the presence of free hydrochloric acid in the stomach of 110 patients, most of whom had various gastrointestinal disorders. The patients, who were in the fasting state, were given 2 tablets of 250 mg. of caffeine sodium benzoate, a gastric secretory stimulant, and one hour later they received Diagnex blue granules (2 Gm.). A urine specimen was taken before the ingestion of the Diagnex blue granules, and 2 hours later a second urine specimen was collected. If free hydrochloric acid were present in the stomach, azure A was released after the oral ingestion of Diagnex blue, and the dye displaced by free hydrogen ions was absorbed in the small intestine and excreted in the urine, where it could be readily detected by the blue or green color it imparted. The results of the Diagnex tests were compared with those of intubation gastric analysis performed with alcohol and histamine in these patients.

Of 39 patients with proved duodenal ulcers, 38 showed free acid and 1 was achlorhydric as revealed by the results of the ion-exchange test, while intubation gastric analysis was negative for free hydrochloric acid in 5 patients. There were no discrepancies between the 2 tests in 8 patients with gastric ulcer. In 21 patients with pernicious anemia, 6 patients with gastric carcinoma, and 4 patients with gastric atrophy proved by biopsy, achlorhydria was revealed by both intubation and tubeless tests. Six patients who had undergone subtotal gastrectomy had positive results from the qualitative ion-exchange test, but one of them failed to show free acid by intubation gastric analysis. Of 26 patients without known gastrointestinal disease, 3 had negative results from the intubation test, while the Diagnex test gave positive results. The qualitative ion-exchange test thus showed a high degree of correlation with intubation gastric analysis. The Diagnex test is a reliable method of differentiating patients with achlorhydria from those secreting free hydrochloric acid. Since intubation is not necessary and because of the simplicity of participation by the patient, ease of interpretation, and cheapness, this method is valuable in the assessment of gastric acid secretion.

Léri's Pleonosteosis: A Study of a Family with a Review of the Literature. J. G. Rukavina, H. F. Falls, J. F. Holt and W. D. Block. J. Bone & Joint Surg. 41-A:397-408 (April) 1959 [Boston].

The typical features of Léri's pleonosteosis, which is a hereditary syndrome, appear to be shortness of stature, Mongoloid facies, short spade-like hands, broad thumbs in valgus position, genu recurvatum, and limitation of motion of the articulations of the body. Pfaundler-Hurler's syndrome, Morquio's disease, and congenital syphilis are most frequently misdiagnosed as Léri's pleonosteosis. This report is concerned with what is believed to be the first American family to exhibit this rare entity. A pedigree, including 4 generations of 21 Caucasian members, was drawn up. It was reported by the relatives that the grandfather of the propositus exhibited the pathognomonic deformity of the hands and feet. His gait was shuffling, and progressive limitation of motion of the joints gradually developed. The mother of the propositus had marked deformities of various joints. Palmar fascitis was present in both hands, in addition to thickening of the fascia of the forearms. Broad thumbs and large toes were associated with flexed, short, stubby fingers and toes. Limitation of motion was found in the neck, shoulders, hips, knees, and elbow joints. The mother walked with short steps. Function of her hands was impaired.

The propositus was an intelligent woman, 43 years of age. The fingers of both her hands were markedly deformed, with flexion deformities, thickening and shortening of the phalanges, and marked limitation of motility. There were flexion deformities of all the toes, with limitation of motion. The range of motion of the elbows, knees, hips, and shoulders was also decreased, while in the neck rotation and flexion were markedly limited. One brother of the propositus was unable to walk with the heels on the ground. He had arthritis of the neck, hands, and wrists and was unable to make a fist, although his hand grip was strong. A similar clinical picture was observed in another brother. These siblings all had a mild Mongoloid slanting of the palpebral fissures; strabismus was present in the sister and one brother. One son of the propositus was free from symptoms of Léri's pleonosteosis, but the other son had most of the symptoms of the syndrome manifested in his antecedents. The most striking osseous abnormality in this family has been the bizarre enlargement of the posterior neural arches of the cervical vertebrae. The hereditary transmission of the gene responsible for Léri's pleonosteosis appears to be autosomal dominant, exhibiting fairly good penetrance and considerable variation in expressivity. Examination of more autopsy material will be required to understand better this syndrome.

Systemic Candidiasis and Endocarditis Due to C. Tropicalis. N. K. Conn, G. P. Crean, A. F. Maccabe and N. Maclean. Brit. M. J. 1:944-947 (April 11) 1959 [London].

The authors report the occurrence of systemic candidiasis due to infection with Candida tropicalis in a 61-year-old woman with dyspepsia of 20 years' duration. On admission to the Western General Hospital in Edinburgh, the patient was grossly undernourished and had marked epigastric tenderness. She had chronic rheumatoid arthritis and a large gastric ulcer. She underwent gastrectomy of Billroth 1 type and was discharged 2 weeks after the operation in good condition, but rigor and vomiting 2 days later made readmission to the hospital necessary. She left the hospital 4 days later against advice, only to be readmitted again 4 days later because of a new attack of fever and vomiting. She was treated with streptomycin and penicillin, and because of persistent vomiting a laparotomy was performed. The stoma was found to be narrowed by a plaque of fibrous tissue projecting into the lumen, and the obstruction was successfully relieved. From the time of the third admission until death, which occurred 57 days later, pus cells were constantly found in the patient's urine, and Escherichia coli, Proteus vulgaris, and Pseudomonas aeruginosa were cultured from catheter specimens. During this period she received 28 Gm. of streptomycin, 28 million units of penicillin, and 8 Gm. of oxytetracycline. Her condition deteriorated, with severe arthralgia, inanition, and anorexia. Blood cultures made during the week preceding death yielded growths of C. tropicalis. A throat swab, a vulvar swab, and a urine specimen obtained 3 days before death yielded growths of C. tropicalis on culture. There was no clinical evidence of mucocutaneous candidiasis at this or any other time.

Autopsy revealed monilial endocarditis, which differed from other reported cases of this condition by (1) the species of the infecting organism (C. tropicalis), (2) the site of the endocarditis with only large vegetations in the right atrium where the blood entering from the inferior vena cava impinged on the endocardium, the valves being unaffected, and (3) the presence of abscesses in the myocardium and in the kidneys, indicating that the infection was septicemic. The case of this patient illustrates the various clinical factors predisposing to the occurrence of systemic candidiasis. Debility and prolonged antibiotic therapy were probably the most important factors in its development. Candida organisms may proliferate in the blood of a patient without any clinical signs of systemic moniliasis appearing other than pyrexia. Unexplained pyrexia occurring in patients with prolonged debilitating diseases, especially those in whom antibiotics and intravenous alimentation have been used, is an indication for culturing the blood in mediums suitable for the growth of fungi.

Symptomless Myelomatosis. G. P. Baker and N. H. Martin. Brit. M. J. 1:953-955 (April 11) 1959 [London].

The authors report on a 43-year-old woman with myelomatosis, in whom 4 years elapsed between the discovery of pronounced hypergammaglobulinemia and the development of signs and symptoms of this disease. The pleural effusion, which brought the patient under observation, was presumed to have been tuberculous and not related to the subsequent myelomatosis, since no further chest complications occurred and the patient's chest remained roentgenologically normal. During the 4-year observation period after this effusion, the patient seemed to be in normal health and carried out all her duties as a housewife. The only clinical abnormality was a mild, orthochromic anemia, which did not increase during this period. Electrophoretic analysis showed increase in gamma globulin, with the sharp peak characteristic of myeloma globulin. The patient's erythrocyte sedimentation rate was persistently increased during the 4 years she continued to attend the outpatients' clinic, until attacks of pain in the lumbar region of the spine and of fever caused her admission to the Mayday Hospital in Croydon, England. Radiography showed osteoporosis and slight collapse of the bodies of several lumbar vertebrae. Considerable albuminuria was observed for the first time, and Bence Jones protein could be detected in the urine. Neither radiotherapy nor chemotherapy with urethan, nitrogen mustard, and tetracycline seemed to influence the patient's illness. The patient died, and autopsy confirmed the diagnosis of myelomatosis by the finding of extensive medullary and extramedullary deposits of plasma cells. There was moderate edema of the lungs, but no evidence of tuberculosis.

Polycythemia and Hydronephrosis or Renal Tumors. J. H. Lawrence and W. G. Donald Jr. Ann. Int. Med. 50:959-969 (April) 1959 [Lancaster, Pa.].

The authors review literature reports suggesting a possible causal relationship between hypernephroma and polycythemia. They saw their first patient in whom hypernephroma was associated with polycythemia in 1940. Since that time, among more than 300 patients with polycythemia, they have seen 2 more with hypernephroma and polycythemia who died of hypernephroma, also one patient with hydronephrosis and fibromyxoma of the kidney and another with hydronephrosis of congenital origin, both of whom had polycythemia and in whom normal blood values resulted from nephrectomy. (The association of polycythemia and hydronephrosis had not been previously reported.) Forssell who was the first to advance the possible causal relationship between hypernephroma and polycythemia has accumulated 20 cases from observation and from the literature. Additional cases presented by Gros, by Conley, and in this report bring the total number with this combination to 27. While polycythemia is far from a constant finding in hypernephroma, and reports of single cases may have no statistical significance, the implication of a relationship is strong.

If one accepts a causal relationship between hypernephroma and polycythemia, then one might postulate an erythropoietic factor produced by the tumor tissue or by the tissue from which it arises. Available reports suggest that it is the exception, rather than the rule, that hypernephroma tissue produces an erythropoietic factor. The association of polycythemia with benign lesions, as reported by DeMarsh in a benign adenoma, by Forssell in polycystic kidneys, and by the authors in 2 cases of hydronephrosis, would seem to indicate that the renal tissue itself has a potential for producing this erythropoietic factor, or that renal involvement—benign, malignant, or infectious—in some unknown way can enhance or possibly cause a polycythemia. The authors briefly review recent experimental work which indicates that a humoral erythropoietic factor is possibly produced by the kidney. The concurrence of polycythemia with hypernephroma and other renal lesions, and particularly the correction of polycythemia after nephrectomy in several cases, would seem to give clinical support to the assumption that the kidney may be a possible source of, or essential to the activation of, a humoral erythropoietic factor, but the method by which this operates is not clear.

The Forme Fruste in Marfan's Syndrome. R. L. Golden and H. Lakin. New England J. Med. 260: 797-801 (April 16) 1959 [Boston].

Marfan's syndrome has been defined as an inherited, autosomal, and dominant connective-tissue defect, primarily involving the skeletal system, the cardiovascular system, and the eye and with multiple clinical manifestations. The skeletal deformities most frequently manifested are dolichostenomelia, arachnodactyly, pectus excavatum (funnel breast), and pectus carinatum (pigeon breast). Also common is the dolichocephalic skull, with long, narrow, pointed face and high palatal arch. Winging of the scapulas is frequently found, as well as hyperextensibility of the joints and pes planus. Ectopia lentis is the most frequent ocular manifestation, but myopia, coloboma, retinal detachment, corneal abnormalities, and congenital mydriasis have also been reported. Cardiovascular phenomena associated with the syndrome are dilatation of the aorta and pulmonary arteries, with resultant valvular regurgitation and dissecting aneurysm. Defect of the interatrial septum is also found in some cases.

The authors call attention to the familial occurrence of Marfan's syndrome, in which recognition of its atypical forms is of special importance. Four members of one family, each with some degree of the forme fruste (atypical form), are described. The first 2 patients were brothers, aged 10 and 7 years, respectively; the third patient was the 23-year-old half-sister of the 2 boys; and the fourth patient was the 50-year-old father of these children. It is pointed out that, when Marfan's syndrome and other hereditary conditions are being considered, the factor of genetic expressivity may be variable from individual to individual, determining the degree of severity of the disorder. Penetrance is the expression of "a statistical concept of the regularity with which a gene produces its effects." A gene may have complete or reduced penetrance, the latter producing the so-called forme fruste, as was true in varying degree of the family discussed. In the absence of the ocular manifestation of the disease (ectopia lentis) in the 2 boys, the identification of the forme fruste was based upon the skeletal and cardiovascular abnormalities and the familial occurrence of the disorder. While patients with Marfan's syndrome are often tall, the 2 boys presented were not. However, relative dolichostenomelia was noted clinically and radiologically, as well as an increase in the length of the extremities in relation to the trunk. It is the skeletal proportions that are important in the syndrome rather than the actual height. Defect of the interatrial septum was suspected in 3 of the cases (the father and 2 boys) and was confirmed at autopsy in one of the boys. The presence of pneumonia in the 2 male siblings confirms previous reports of its frequency in association with this syndrome.

Although knowledge of the manifestations of Marfan's syndrome is widely disseminated, too often only the syndrome in its classic form is diagnosed. The authors feel that the practitioner must be alerted to the forme fruste and the importance of family history and examination in arriving at a diagnosis. Early recognition of the syndrome will enable its graver aspects—for example, the cardiovascular lesions—to be treated. Moreover, study of the family of an affected individual would determine the extent of transmission of the disease. A patient with the forme fruste could transmit the full clinical syndrome.

Tietze Syndrome: A Report of Four Cases. A. J. McSweeney. Wisconsin M. J. 58:223-227 (April) 1959 [Madison].

Although Tietze reported the syndrome of painful enlargement of the costal cartilages in 1921, American reports on this disorder did not begin to appear until 1953, but since then at least 38 cases have been reported in the United States. The disorder has been variously referred to as painful nonsuppurative swelling of costochondral cartilages, chondropathia tuberosa, costochondral syndrome, costal chondritis, sternochondralgia, and prominent costal cartilages. Various forms of treatment have been employed. The application of heat locally and the use of analgesics may provide symptomatic relief. Deep x-ray therapy, nitrogen mustard, local infiltration with procaine, corrective postural exercises, use of bedboards, and surgical removal of the involved cartilage have been advocated. Since the costochondral syndrome is a benign and self-limited condition, therapeutic measures should not be too radical. The author found that oral steroid therapy is a simple and effective remedy. He presents the histories of 2 men, aged 35 and 22 years, in whom painful enlargement at the costochondral junction responded to the oral administration of prednisolone. After citing investigators who have resorted to the local injection of hydrocortisone in treatment of Tietze's syndrome, he tabulates 12 cases (including the 2 mentioned) in which steroid therapy was used.

The author also presents the histories of 2 women, aged 51 and 27 years, with painful enlargement of the costochondral junction, who were not treated with steroids. In the older woman, the discomfort was relieved by propoxyphene, and in the younger one it disappeared gradually without treatment. Since the results of treatment with oral administration of prednisolone compare favorably with those of local hydrocortisone injection, further trial of orally administered steroids in the treatment of painful nonsuppurative swelling of costochondral cartilages seems warranted.

SURGERY

Radiosurgical Treatment of Primary Malignant Tumors of the Base of the Tongue. F. Brunetti. Minerva chir. 14:207-212 (Feb. 28) 1959 (In Italian) [Turin, Italy].

Primary malignant tumor of the base of the tongue was present in 62 out of 1,438 patients with malignant tumors, who were hospitalized at the otorhinolaryngologic clinic of the University of Turin between 1936 and 1958. Spindle-cell carcinoma was present in 24 patients, basal-cell carcinoma in 18, reticulosarcoma in 2, and thyroid adenocarcinoma in 2. Most of the patients were from 50 to 70 years of age. At the time of admission, the lesion was localized at the base of the tongue, with involvement of adjacent anatomic structures, in 38 patients; the tumor invaded the epiglottis and pharynx in 15 patients, the palatine tonsil in 6, and the body of the tongue in 3. There were 36 instances of the vegetative type of tumor and 26 of the infiltrative type.

During the first period (1936-1949), of 24 patients with localized primary tumor at the base of the tongue, roentgenotherapy was given to 16; radium implantation, preceded by immobilization of the tongue by Soerensen procedure, was performed on 4; and a median pharyngotomy, followed by electrosurgical resection, was carried out in 4. Subglossopharyngolaryngotomy was performed on 4 patients with glossolaryngeal tumor, and radium implantation through the mouth was carried out in 2 patients with glossotonsillar tumor. During the second period (1950-1953), roentgenotherapy was given to all patients with primary malignant tumor of the base of the tongue and with involvement of the adjacent areas. A subglossopharyngolaryngotomy was performed on 2 patients with glossolaryngeal tumor. Radium implantation through the mouth, preceded by immobilization of the tongue by the Soerensen procedure, was carried out in 3 patients, and a median pharyngotomy, followed by electrosurgical resection, was performed on 2; all 5 patients had a primary malignant tumor localized at the base of the tongue.

During the third period (1954-1958), roentgenotherapy was the only procedure used in patients with primary malignant tumor of the base of the tongue and with involvement of the adjacent areas. This procedure was preceded in many instances by unilateral or bilateral exeresis of the lymph nodes. This method consists in administering a course of radiation in a total dose of 6,000 r of either radiocobalt (Co^{60}) or roentgen rays. Patients with primary malignant tumor of the base of the tongue alone have been recently treated under general anesthesia by a lateral buccopharyngotomy and exeresis of the lymph nodes, followed by radium implantation under direct vision. This method allows an accurate evaluation of the extent in width and in depth of the neoplastic lesion. Of 22 patients available for follow-up during the past 8 years, death involved 3 with glossopharyngeal tumor, 1 with tumor of the base and involvement of the body of the tongue, and 1 with tumor of the base of the tongue, who underwent lateral buccopharyngotomy. The survival data are too recent to warrant any interpretation.

Mitral Restenosis. G. C. Patterson and J. R. Marshall. Brit. Heart J. 21:174-176 (April) 1959 [London].

The authors report on 7 patients, between the ages of 23 and 41 years, who were operated on for mitral stenosis and in whom restenosis of the mitral valve was confirmed at a second operation. These patients were observed among 400 patients operated on for mitral stenosis at the Royal Victoria Hospital in Belfast, Northern Ireland. Symptoms recurred at intervals, ranging from 8 to 41 months, after the initial valvotomy. A second operation was followed by improvement in 6 patients. One patient failed to improve and died 3 months after the operation. In 4 patients no evidence of rheumatic activity was found during the period of observation before and after surgical intervention. It is suggested that rheumatic fever may not be the only causative factor concerned in mitral restenosis.

Diagnostics, Indications for and Operative Closure of Septum Defects of the Heart with the Aid of Hypothermia and Extracorporeal Circulation. F. S. P. van Buchem, J. Nieveen, L. B. van der Slikke and others. Arch. chir. neerl. 11:15-40 (no. 1) 1959 (In English) [Arnhem, Netherlands].

The authors discuss the pathological anatomy of atrial septal defects (A. S. D.) and of ventricular septal defects (V. S. D.), the clinical picture of A. S. D. and the indications and contraindications for the surgical treatment of A. S. D., and the clinical picture of V. S. D. and the indications for surgical closure of V. S. D. Aids used in the operative closure of A. S. D. and V. S. D. are evaluated, particularly those used in the Groningen Thorax Center. After outlining the technique used in the closure of septal defects of the heart, the authors tabulate and discuss data on patients treated by them. In 40 patients with isolated septal defects (32 A. S. D. and 8 V. S. D.), they used extracorporeal circulation 14 times (6 times in A. S. D. and 8 times in V. S. D.). The other patients with A. S. D. were operated on with the aid of hypothermia. There were 4 deaths, 1 in a patient with A. S. D. and 3 in patients with V. S. D.

The authors feel that under hypothermia of from 29 to 30 C (84.2 to 86 F) not too complicated atrium secundum defects can be closed with relative safety. In the Groningen center the heart-lung machine of Lillehei-De Wall functioned satisfactorily in 14 children whose weight did not exceed 20 to 25 kg. (44 to 55 lb.), with a minute volume of 50 to 70 ml. per kilogram of body weight. The greater minute volumes required for larger patients is possible with the Lillehei apparatus, but in the Groningen center experimental studies are being carried out to determine what combination of oxygenators and pumps will give the best results. It is an established fact that success depends not only on the type of machine but equally on good teamwork. There are many problems still to be solved, but it may be assumed that further progress will be made in intracardiac surgery. Particular attention will have to be paid to the problems of hemolysis, destruction of thrombocytes, defibrination, fibrinolysis, and denaturation of proteins during perfusion.

The use of potassium citrate to arrest the heart may sometimes have more disadvantages than advantages by causing a delay in the recovery of the myocardium. The construction of the heart-lung machine must be greatly simplified. A minimal perfusion might be sufficient if a substance could be found with a reversible effect on the oxidation processes within the tissues. The combination with hypothermia, even if cooling is not so drastic as formerly, still involves the risk of a possible ventricular fibrillation. Although it is possible to stop this by means of a defibrillator, the subsequently necessary massage of a heart in which repairs have been carried out seems less desirable, especially if Ivalon has been used to cover the defects. In the repair of defects of the atrial septum the authors used a chemically controlled hypothermia of ± 30 C (86 F), and the results were favorable. Metabolic acidosis could be corrected by the intravenous administration of 4.2% of sodium bicarbonate, while the anesthetist regulated his ventilation technique according to the results of the chemical investigation.

Semeiology of Substernal Adenoma of the Thyroid. W. O. Lodge. A. M. A. Arch. Otolaryng. 69:419-423 (April) 1959 [Chicago].

Substernal adenoma is of insidious onset and of long duration. Although it is comparatively rare, it enters into the differential diagnosis of cancer of the lung but has a far better prognosis. In the course of numerous consultations and 325 biopsies and tracheal decompressions, the author met with 7 cases in which goiters were not palpable in the neck but were occult and intrathoracic. In 1 patient the goiter was inoperable, but 6 patients were operated on successfully and survived. The author reviews the manifestations of substernal adenoma in the light of recent studies by Soulas and Mounier-Kuhn; these investigations have dispelled the idea that early substernal adenoma produces no symptoms but dyspnea on exertion. He now realizes that to look only for respiratory symptoms is a mistake.

As to where one must look for the first signs of retrosternal adenoma, he says that a review of his own cases has convinced him that the answers are in the veins and in the manifestations of venous back pressure. In this connection he points out that another investigator observed hemoptysis in 3 of 15 cases. The trachea derives its blood supply from the inferior thyroid arteries. In the presence of substernal adenoma the inferior thyroid arteries, innominate veins, and superior vena cava soon become congested, as evidenced by distention of the superficial veins of the neck and thorax.

The author mentions the case of a pregnant woman in whom venous congestion of the head and neck, as well as radiology, led to the diagnosis of substernal adenoma of the thyroid. He also cites the case of a colleague who had dilated capillaries on the face and neck, which turned blue in cold weather. Within the nose a vascularized area on the nasal septum was evidently responsible for epistaxis, which caused the patient's admission to hospital. Tomograms demonstrated a large calcifying soft-tissue mass at the level of the thoracic inlet; this mass compressed the right lateral wall of the trachea. The radiologist suggested that a similar picture may be presented by a calcifying adenoma of the thyroid. At operation a calcified adenoma of the thyroid was excised. Investigation of epistaxis or hemoptysis may bring to light this occult but innocent tumor, which may be dealt with by surgical intervention with minimal mortality.

Treatment of Cancer of the Lung. C. Crafoord. Acta Unio internat. contra cancrum 15:443-447 (no. 2) 1959 (In English) [Louvain, Belgium].

The author believes that the most important diagnostic procedure in the detection of cancer of the lung is unquestionably conventional roentgenologic examination. As soon as any patient has clinical signs or symptoms suggestive of development of bronchial carcinoma, his chest should be x-rayed. If a tumor is in the process of development, the chest films will give valuable guidance with respect to both its localization and its etiology. The bronchoscopist can, in a large percentage of cases, provide the pathologist with specimens which permit a microscopic diagnosis. In 80% of all patients treated by the author, biopsy was possible. In those in whom investigation by biopsy is not possible, exploratory thoracotomy should be performed. This applies even if such measures as sputum examination, examination of local bronchial washings, and needle biopsy give negative results.

All the patients treated by the author underwent thorough clinical and laboratory examinations, as well as tests of pulmonary and cardiac function and roentgenologic investigation, before the question of operation was decided. Patients in whom distant metastases which could not be removed surgically were present were considered to have inoperable disease. This also applied to those whose ventilatory function was impaired. When circulatory disturbances were present, the patient's tolerance to blocking of the pulmonary artery on the affected side was tested, both at rest and during exercise, before operation was recommended. If investigation indicated that there was a considerable risk of cor pulmonale, surgery was advised against. Despite roentgenologic examination of the thorax and other organs, as well as of the skeleton, it was not always possible to diagnose the presence of distant metastases, and for that reason exploratory operation was performed in a large percentage of cases. Advanced age was also considered to be a contraindication for surgery.

In carrying out this operative procedure, each pulmonary lobe was regarded as a separate unit. The decision to perform total extirpation of the lung, or lobectomy, has therefore been based on whether the cancer has spread to more than one lobe by direct invasive growth, or whether lymph node metastases were present other than locally in the hilar region of each lobe. Exceptions to this rule were only made when the patient was elderly or when the respiratory function had been greatly impaired. Palliative lobectomy was then performed, even when metastasis had taken place to lymph nodes beyond the hilar region of the lobe in question. In such cases, operation has been as radical as possible with respect to dissection of the lymph nodes in the hilus and mediastinum. Radical or superradical pneumonectomy with ligation of the intrapericardial vessels and resection of the pericardium and all areolar tissue, together with the mediastinal lymph nodes, has been done only in cases of invasive growth beyond the region of the lung, towards the mediastinum and pericardium. This operation has not brought about any marked improvement in the 5-year survival rate. It has instead shown a tendency to increase the primary mortality.

Certain Problems of Surgical Treatment in Cardiac Aneurysms. B. V. Petrovsky. Khirurgiya 35:33-39 (no. 4) 1959 (In Russian) [Moscow].

The author reports on 6 patients with cardiac aneurysm who were successfully operated on. In 3 of these the author used an original operation devised by him. The operation consists of utilizing a pedunculated diaphragmatic flap. The flap is laid on and sutured over the aneurysm. The advantages of the operation are the strengthening, on the one hand, of the sutured myocardial wall of the aneurysm with diaphragm muscle and, on the other, the resulting improvement of the blood supply of the myocardium. Attention is called to the fact that innervation and blood supply of the diaphragm and the pericardium are related to one another through the pericardiophrenic arteries and nerves. The "take" of the muscular diaphragmatic flap with the myocardium results in gradual compensatory adaptation of the flap and its participation in the work of the heart.

Early and Late Hemodynamic Effects of Mitral Commissurotomy. W. S. Lyons, R. G. Tompkins, J. W. Kirklin and E. H. Wood. J. Lab. & Clin. Med. 53:499-516 (April) 1959 [St. Louis].

The authors report the hemodynamic data from 9 women and 3 men, between the ages of 23 and 52 years, with mitral stenosis, who underwent mitral commissurotomy between April, 1951, and October, 1952, and who accepted catheterization of the right heart 3 times or more, i. e., one week before commissurotomy, 10 to 90 days after, and 8 to 30 months after satisfactory mitral commissurotomy. Although every patient in this series obtained definite clinical and objective hemodynamic benefit after mitral commissurotomy, each had some degree of residual stenosis after the operation. All the patients were followed up for periods ranging from 4½ to 6 years after the operation, and the clinical improvement was maintained by 9.

Evidence both clinical and objective (from repeated catheterization and operation) of the recurrence of the preoperative stenotic condition was found in 3 of the 12 patients 3 to 5 years after commissurotomy. Recurrence of stenosis cannot be clearly proved without cardiac catheterization soon after the operation to establish on an objective basis the actual degree of relief of stenosis obtained by the operative procedure. Both accuracy and completeness are essential in these measurements. When the measured and derived data from determinations of blood pressure and flow were compared with the clinical status of the 12 patients before and after operation, significant correlation was apparent.

Profound Hypothermia. C. E. Drew, G. Keen and D. B. Benazon. Lancet 1:745-747 (April 11) 1959 [London].

The authors report experiments on dogs which were performed in an attempt to produce profound hypothermia by blood stream cooling. A simple extracorporeal circuit containing 2 reservoirs, one to collect pulmonary venous blood from the left atrium and the other to collect systemic venous blood from the right atrium, was employed. The animals were anesthetized with thiopental sodium and succinylcholine, and were given nitrous oxide and oxygen from an automatic oxygenator. The chest of the animal studied was opened by bilateral transsternal thoracotomy, and a catheter as large as possible was inserted in the left atrium and connected by the pulmonary venous line to the left atrial reservoir. An appropriate pump was then started, and blood from the left atrial reservoir was passed through a cooling coil and then returned to a femoral artery through one head of the pump-unit. Blood from the systemic venous or right atrial reservoir was pumped through the other head of the pump into the pulmonary artery by way of a cannula inserted through a stab incision in the infundibulum of the right ventricle. Systemic venous blood was not cooled.

A small number of experiments was sufficient to show that with the use of this simple apparatus it was possible to induce profound hypothermia (from 37 C [98.6 F] to 8 C [46.4 F]) in 2 dogs, followed by complete circulatory arrest for 30 minutes, and then to rewarm them with recovery. In a second series the apparatus was modified with an improved heat-exchanger, instead of a coil, and pump-heads of the DeBakey type, instead of the sigmamotor pump-heads used in the previous experiments. To prevent sudden hypotension at the onset of partial left ventricular bypass, an adjustable clip was placed on the pulmonary venous line, so that drainage from the atrium could be controlled by the surgeon. The flow of chilled blood into the aorta was started slowly, and increased to its maximum of 50 to 70 cc. per kilogram per minute at the onset of right ventricular bypass. The rate of increase in flow through the extracorporeal circuit was governed by the blood pressure, which was kept at an arbitrary mean of 80 to 100 mm. Hg. Two of the 4 dogs in which cooling was carried out to 15 C (59 F), followed by a period of complete circulatory arrest lasting 20 to 45 minutes before rewarming, survived without evidence of neurological damage.

Profound Hypothermia in Cardiac Surgery: Report of 3 Cases. C. E. Drew and I. M. Anderson. Lancet 1:748-750 (April 11) 1959 [London].

Using the technique of inducing profound hypothermia with cooling to 15 C (59 F) described in the preceding paper, the authors operated on 3 children, a 12-month-old Mongoloid boy, a 4-year-old high-grade Mongoloid boy, and a 2½-year-old boy, all with congenital intracardiac defects. After a period of total circulatory arrest of 46 minutes, the first patient appeared to be recovering; 70 minutes after the chest had been closed, the infant was breathing spontaneously, moving all 4 extremities and swallowing. However, 45 minutes later this patient died of heart block after partial correction of a persistent atrioventricular canal of the complete variety. The other 2 patients survived. The 4-year-old boy had right atriotomy and ventriculotomy for obliteration of an atrial and ventricular septal defect. Repair of the latter necessitated resection of the medial cusp of the tricuspid valve and its resuture. In this patient the total circulatory arrest lasted 45 minutes. The second surviving patient had a repair of a ventricular septal defect which required circulatory arrest for 25 minutes. In none of the patients did ventricular fibrillation occur. Hemolysis was negligible, and there were no significant biochemical upsets. The survivors did not show any evidence of neurological or other damage and made uneventful recoveries.

Since this paper was submitted for publication, 4 additional patients have been operated on with the aid of profound hypothermia for the correction of intracardiac defects. One patient, an infant weighing 8 lb. (3.6 kg.), died 24 hours after the operation; his death was probably due to heart block. One of the 3 survivors was a 49-year-old patient who had complete cardiac arrest for 42 minutes at a temperature of 15 C. Greater experience may confirm the authors' growing belief that profound cooling with cardiac bypass will play an increasing part in intracardiac surgery at the expense of cardiopulmonary bypass at normal temperatures, with use of a pump-oxygenator.

Bilateral Internal Mammary Arteries Ligation in the Coronary Artery Disease. M. Battezzati, A. Tagliaferro and A. D. Cattaneo. Sc. med. ital. 7:463-485 (no. 3) 1959 (In English) [Rome].

Anastomotic connections exist between the coronary system and the internal mammary arteries. Ligation of both internal mammary arteries at the second intercostal space, i. e., beyond the origin of the main collateral branches, enhances the development of these anastomoses as a substitute collateral system in coronary disease. The mechanism of the vicarious action consists in diverting the blood flow from the mammary artery into its collateral branches, so that the total flow through the latter is increased; this is further intensified by coronary hypotension and myocardial hypoxia.

The degree of protection afforded by the bilateral ligation of the internal mammary arteries in coronary occlusion was studied in 50 dogs in which infarction was produced by ligation of the anterior descending branch of the left coronary artery at about 3 mm. from its origin. The animals were divided into 2 groups of 25 each; bilateral ligation of the internal mammary arteries was performed 15 minutes after the ligation of the anterior descending branch of the left coronary artery in both groups, and in the second group the bilateral ligation of the internal mammary arteries was performed at the level of the third intercostal space. The survival rate in the first group of animals was 80%, and in the second group it was 76%. Hemodynamic studies carried out on the dogs have shown that the ligation of the mammary arteries tends to restore to normal the circulatory conditions seriously altered by coronary occlusion.

Bilateral ligation of the internal mammary arteries was performed at the second intercostal space on 207 men and 97 women, between the ages of 33 and 83 years; of these 304 patients, 151 (49.6%) had angina pectoris and 153 (50.4%) had myocardial infarction, associated or not associated with angina pectoris. The coronary disease was accompanied by symptoms of cardiac failure in 230 patients (75.6%). Of the 304 patients, 288 (94.7%) were improved within 30 days after the surgical intervention, 15 (4.9%) were therapeutic failures, and 1 (0.3%) had died. The improvement generally persisted for a period ranging from 1 month to 3 years after the surgical intervention. Twelve patients died within this period. Of the total number of 13 deaths, 8 resulted from heart disease and 5 from extracardial causes. None of the patients died in the course of the operation. One hundred ninety-five patients (64.1%) showed electrocardiographic improvement affecting the voltage, S-T segment, T wave, and rhythm. The bilateral ligation of the internal mammary arteries, like any other surgical procedure causing revascularization, does not provide the patient with a new heart but has the advantage of offering the same results as other more complex and radical surgical procedures, with less difficulty for the surgeon to perform and with less risks and trauma for the patient.

Bilateral Internal Mammary Artery Ligation and Coronary Artery Occlusion. R. Hardin, H. B. Shumacker Jr., Chien Sheng Su and G. Bounous. Surg. Gynec. & Obst. 108:518-522 (May) 1959 [Chicago].

Healthy mongrel dogs were used for the experiments described. In one group of animals, ligation of the internal mammary arteries was performed through a transverse midsternal incision at the level of the second intercostal space. Both arteries were identified and divided between ligatures. Another group of animals was subjected to a similar incision and dissection, but no ligation was performed. In both groups of animals, ligation of the anterior descending branch of the left coronary artery was carried out one month later. In a third group of animals subjected to no previous surgery, the same coronary artery ligation was accomplished. Postmortem study was performed when the dogs died or when they were killed 7 days after coronary division.

These animal experiments failed to demonstrate that bilateral ligation of the internal mammary arteries performed one month previously provided any protection against division of the anterior descending branch of the left coronary artery. The survival rate was quite as good in untreated controls and in animals previously subjected to a sham operation. No increase in retrograde coronary flow was demonstrated in animals a month after bilateral internal mammary ligation as compared with animals in the other 2 groups. The authors conclude that these experiments and a survey of those reported in the literature yield no convincing experimental basis for applying the procedure of internal mammary artery ligation to man.

Experimental Evaluation of Internal Mammary Artery Ligation as a Method of Myocardial Revascularization. J. H. Vansant and W. H. Muller Jr. Surgery 45:840-847 (May) 1959 [St. Louis].

Three experimental approaches were utilized to determine whether or not internal mammary artery ligation increases collateral blood flow to the heart. 1. The mortality rate following ligation of a major coronary artery was employed to judge the degree of protection afforded the heart. A mortality rate of 90% occurred in the control group. Following ligation of the internal mammary arteries, the mortality rate was 70%. These results are not indicative of statistically significant myocardial protection. 2. A technique was devised to measure simultaneously pressures in the internal mammary artery and pressures and flows in a tributary of this vessel which is comparable to the pericardiacophrenic artery. Occlusion of the internal mammary artery distal to the tributary did not significantly affect the pressures in the internal mammary artery or in the tributary; neither did it appreciably increase the volume flow through the tributary. 3. The third method of evaluation consisted of measuring the acute effects of bilateral internal mammary artery ligation on the retrograde pressures and flows of an occluded coronary artery. No significant change in either measurement occurred when the internal mammary arteries were totally obstructed. No evidence was obtained from these studies to demonstrate that bilateral internal mammary artery ligation increases the collateral blood supply to the myocardium.

Coronary Heart Disease: III. Chronic Arrhythmias as Influenced by the Beck Operation. B. L. Brofman, J. F. Bond and D. S. Leighninger. Am. J. Cardiology 3:618-625 (May) 1959 [New York].

The authors selected from 350 patients, who underwent the Beck operation for relief of coronary artery disease, 20 in whom a chronic arrhythmia was observed as a prominent manifestation of coronary heart disease before the operation, and who were followed up for 1 to 6 years after the operation. In 15 of these 20 patients ventricular extrasystoles were prominent before the operation; auricular extrasystoles were present in 3, and sinus tachycardia in 2. Long-term follow-up revealed significant clinical improvement, associated with abolition or diminution of the arrhythmia in 17 (85%) of the 20 patients. Within the limits of this study, these arrhythmias represented a reliable index of myocardial ischemia in a given patient with coronary heart disease. The consistent abolition of the arrhythmias with concomitant clinical ("subjective") improvement constitutes confirmatory ("objective") evidence of the beneficial effect of the operation. During and after the operation, administration of digitalis had a specific inotropic and chronotropic influence on the heart, with decreased instability, reduced incidence of paroxysmal arrhythmias, and increased stroke output. Digitalization is, therefore, recommended before the surgical intervention for coronary artery disease.

Sarcoma of Esophagus: Surgical Treatment. J. Borrie. J. Thoracic Surg. 37:413-426 (April) 1959 [St. Louis].

In a search of the literature the author found 19 patients who had been operated on for esophageal sarcoma. He reports another case, that of a 63-year-old man with a polypoid fibrosarcoma of the lower third of the esophagus; this condition was detected 8 months after a transthoracic repair of a hiatus hernia, previously performed at another hospital, and 1 month after the onset of dysphagia. The patient was subjected to a partial esophagogastrectomy, with esophagogastrostomy and block dissection of the regional lymph nodes, at Dunedin (New Zealand) Hospital, and is now well, 6 years after the operation. The history of this patient has suggested that the tumor was not present at the time of the radical operation for hiatus hernia. Its detection 8 months later emphasizes the fact that esophageal tumors often do not cause symptoms, and that sometimes they do occur in association with hiatus hernia. It is important that all patients presenting hiatus hernia should be subjected to esophagoscopy before the operation. The recurrence of dysphagia after a successful herniorrhaphy should not be ignored, but should be promptly and repeatedly investigated by esophagoscopy as well as by esophagrams. The possibility of sarcoma of the esophagus should be borne in mind in patients manifesting dysphagia after an apparently successful hiatal herniorrhaphy. If the tumor is polypoid in type, and if it is detected early, the chances of recovery after a successful resection are excellent.

Pulmonary Abscess: A Study of 70 Cases. D. N. Pickar and W. F. Ruoff. J. Thoracic Surg. 37:452-459 (April) 1959 [St. Louis].

The authors report on 70 patients with pulmonary abscesses treated at the Veterans Administration Hospital in Louisville, Ky., during the past 10 years. The patients were males, 59 whites and 11 Negroes, ranging in age from 20 to 60 years. Patients with abscesses resulting from tuberculosis, fungous or parasitic infection, and carcinoma were not included in this study. The duration of symptoms before hospitalization varied from 1 month or less up to 26 months. Sensitivity studies were performed on the sputum of all the patients. The choice of the antibiotic varied. Penicillin alone was administered to 21 patients; penicillin with tetracycline, to 12; penicillin and streptomycin, to 3; tetracycline alone, to 1; and streptomycin combined with isoniazid, to 1 (because of the possibility of tuberculosis). Forty-four patients were treated with medicaments. Thirty-five patients were considered to have closed cavities after 10 to 120 days of this medical treatment. The cavities of the remaining 35 did not close, and 24 of these were operated on. Twelve patients in all died, representing a mortality of 17.1%.

Pulmonary abscesses are considered to be primarily a medical problem, and if even a slight improvement is obtained during treatment with medicaments, it should be continued for a prolonged period. Surgical procedures should be carried out only on patients in whom medical treatment has failed. The advent of antibiotics and improvements in anesthetization and surgical techniques have substantially improved the prognosis in patients with pulmonary abscesses. A long period of hospitalization is required, however, and the disease remains a grave problem.

Surgical Diagnosis of "Chronic Pancreatitis" and Chronic Relapsing Pancreatitis. M. A. Birnstingl. Brit. M. J. 1:938-943 (April 11) 1959 [London].

The authors report on 18 men and 4 women with nonmalignant chronic pancreatic disease, the presence of which was confirmed at surgical exploration. These 22 patients were divided into 2 groups, one consisting of 11 men and 1 woman, whose ages at the onset of symptoms varied between 41 and 82 years, and the other consisting of 7 men and 3 women, whose ages at the onset of symptoms varied between 18 and 65 years. Jaundice of obstructive type was present in 10 of the 12 patients in the first group. The duration of this symptom before operation varied between 2 and 18 weeks, and it formed the main indication for surgical exploration. The pathological diagnosis of "chronic pancreatitis" was based on the findings at surgical exploration, supplemented by a surgical biopsy including small pieces of tissue removed from the surface of the pancreas in 8 patients. Surgical procedures in 10 of the 12 patients were undertaken to relieve biliary obstruction by internal drainage. The remaining 2 patients did not undergo further surgical intervention. The clinical findings in this group of 12 patients were strongly suggestive of malignant disease. This likelihood was supported by the age of the patients and the short duration of their illness. The findings at operation provided further presumptive evidence of the presence of carcinoma, since they included the presence of a tumor in the pancreas in 9 patients, 7 of whom had obstructive jaundice. Nevertheless, the histological report of "chronic pancreatitis" led to its acceptance as providing the most likely diagnosis of the true nature of the disease. All 12 patients died of carcinoma of the pancreas within 4 days to 3 years after exploration; only 2 patients survived more than 1 year. An important cause of error in the pathological diagnosis was a failure to recognize the structural effects of pancreatic ductal obstruction. The term "chronic pancreatitis" is an inaccurate description of this type of pathological change.

The clinical picture of the 10 patients in the second group was one of chronic relapsing pancreatitis. The average age of these patients at the onset of symptoms was 45 years, i. e., 15 years less than the average age of the patients in the first group. The clinical picture was supported by the macroscopic findings at exploration and by a postoperative survival time varying between 6 and 40 years. A barium-meal examination was carried out in 6 of the 10 patients, and changes in the configuration of the duodenal loop were observed in 5. Pancreatic calcification was present in 4 patients. The macroscopic and microscopic changes observed in pancreatic biopsy specimens obtained from 4 of the patients were consistent with the probable origin of these changes as a sequel to recurrent inflammatory incidents in the parenchyma. The evidence produced by other workers suggested that in a large proportion of cases the pancreatic calcification in relapsing pancreatitis occurs within the ducts and not in the parenchyma, representing an effect rather than a cause of the disease. In the author's patients with relapsing pancreatitis the effects of pancreatic ductal obstruction were not seen, but direct pancreatographic procedures were not considered justifiable in these patients, and, therefore, it was not possible definitely to exclude an obstructive causative factor.

Cancer and Diverticulitis of Transverse Colon: Coexistence. H. M. Moguillanes and M. G. Mendoza. Prensa méd. argent. 45:3290-3294 (Oct. 10) 1958 (In Spanish) [Buenos Aires].

The association of chronic diverticulitis of the transverse colon with cancer of that segment is rare. Each disease has an aggravating influence on the other. A man, 58 years old, with rectal disorders of long duration and acute anemia was hospitalized. During the previous 9 months the patient had had rectal hemorrhages, and he had lost 13 kg. (28½ lb.) in weight. Examination of the large intestine with opaque enema showed multiple diverticula in the transverse colon and a stricture at the center of the segment. An exploratory laparotomy showed chronic diverticulitis of the entire transverse colon and a tumor in the center of the segment. The tumor was the size of an orange and of a carcinomatous aspect and infiltrated the visceral serous layers. The operation to which the patient was subjected consisted of resection of the transverse colon and the ascending colon, including the tumor, with an anastomosis of the ileum and the descending colon. His immediate and late postoperative courses were uneventful, and he was discharged 3 weeks after the operation in satisfactory condition. The anatomicopathological examination of the surgical specimen showed a large number of diverticula in the colon and carcinoma of the mucosecreting type.

Intra-Aortic Nitrogen Mustard Therapy in Advanced Pelvic Malignancies. R. L. Byron Jr., B. P. Singh, H. R. Bierman and K. H. Kelly. Surgery 45:634-641 (April) 1959 [St. Louis].

Injection of a nitrogen mustard, such as mechlorethamine hydrochloride (HN_2), into the nutrient artery of a malignant tumor has been used as one point of direct attack. The studies described were designed to investigate the effect of intra-aortic nitrogen mustard therapy in advanced pelvic malignancies. The investigations were carried out by a team of surgeons, internists, anesthetists, and a radiologist. Thirty-four patients with advanced pelvic malignancies of various types comprised the material for this study. Carcinoma of the cervix, ovary, and rectum or sigmoid accounted for 27 of the 34 lesions. The diagnoses were confirmed by at least one biopsy. Thirty of these 34 patients had been previously treated by definitive radiation therapy and/or surgery. The remaining 4 patients had not received any previous therapy.

Thirty-one patients were subjected to a pelvic laparotomy. After manual exploration, the aorta, just above its bifurcation, and the inferior vena cava were exposed, and Penrose rubber drains were placed around them to serve as tourniquets. The arterial circulation in both lower extremities was occluded by femoral artery pneumatic tourniquets. After the occlusion of the femoral arterial circulation, a single injection of freshly prepared nitrogen mustard (HN_2) was rapidly given into the aorta just above its bifurcation. During and after the injection, the aorta and the inferior vena cava were occluded above the injected site for 5 minutes. This allowed maximum arterial concentration of the nitrogen mustard in the tumor-bearing area of the pelvis. After the 5-minute period all the tourniquets were released, and the abdomen was closed. Three patients were treated by the arterial catheterization technique in which the left brachial artery was used. The artery was exposed, and loops of rubber bands were placed around the vessel above and below the site for the opening of the artery. An incision was made through the wall of the artery, and the tip of the catheter was inserted and then guided into the descending aorta by roentgenoscopy to a point just above the aortic bifurcation. The catheter was left in place, and the patient returned to the ward. After the occlusion of the femoral arterial circulation, nitrogen mustard was injected through the catheter. The occlusion was maintained for 5 minutes after the injection and then released. The catheter was left in the artery 5 days without untoward effect.

The injection of nitrogen mustard into the nutrient artery has proved of some value in the palliation of advanced pelvic malignancies. Seven of 34 patients showed objective improvement; there were 3 postoperative deaths. Patients with malignant tumors localized to the pelvis, which are not amenable to surgery or irradiation, are suitable for intra-aortic nitrogen mustard therapy. This is particularly true when the tumor has involved the lateral pelvic walls. The final decision to utilize chemotherapy frequently must be made at the operating table during the exploratory laparotomy. The nitrogen mustard can be administered safely via the aorta in doses of 0.25 to 1.3 mg. per kilogram of body weight.

Carcinoma of the Corpus Uteri. W. Hawksworth. Acta Unio internat. contra cancrum 15:270-275 (no. 2) 1959 (In English) [Louvain, Belgium].

The author reports on 251 patients with carcinoma of the corpus uteri seen in the area department of obstetrics and gynecology at Oxford, England, between 1940 and 1957. Of these 251 patients, 220 were treated surgically, with an operative mortality of 60. One hundred sixty-five patients were followed up 5 years after the initial treatment, and 105 of these are still alive. Of the 151 patients in the follow-up group who were operated on, 124 showed no evidence macroscopically of extension of growth beyond the uterus at the time of operation, and 95 of these are living 5 years after the operation. There were, however, 27 patients with macroscopic evidence of spread beyond the uterus at the time of operation, and only 8 have survived 5 years. Of the 60 patients who died during this period, 38 had recurrence, but in the whole group of 251 patients only 3 had recurrence in the vaginal vault. The commonest sites of recurrence are the lymph nodes of the pelvic walls. The author considers that operation should include lymphatic dissection as a routine treatment. The increase in surgical risk is low, but the prognosis with positive pelvic lymph nodes is bad. The author claims a staging of the disease based on operative findings rather than the actual clinical classification.

Cytologic Diagnosis of Rectal and Colonic Conditions. B. M. Chapman. Gastroenterology 36:501-504 (April) 1959 [Baltimore].

This report is concerned with an analysis of cytological diagnosis in rectal and colonic conditions from material accumulated over a period of 10 years. A total of 877 smears from 746 patients were studied. The preparations were taken during sigmoidoscopic examinations when disease was seen or suspected. Ninety-two of the smears were positive, 2 falsely positive, 12 falsely negative, 10 suspicious, and 4 falsely suspicious. Of the 92 positive smears, 66 were proved by biopsy or examination of the surgical specimen to be adenocarcinoma, and 6 malignant adenoma. In 18 patients with positive smears, follow-up information could not be obtained. With the deletion of this group from the analysis, it is found that the accuracy of cytological diagnosis in this series was 77%. Study of the smears proved valuable as an adjunct in the diagnosis of other conditions of the rectum and colon, such as ulcerative colitis, amebic dysentery, bacillary dysentery, diverticulitis, and tuberculosis. The test appears to have its greatest value in the diagnosis of lesions between the splenic flexure and the rectosigmoid.

NEUROLOGY & PSYCHIATRY

The Treatment of Tuberculous Meningitis in Adults from 1947 to 1957. F. Russi, G. Rossi and R. Bonazza. Minerva med. 50:606-618 (Feb. 28) 1959 (In Italian) [Turin, Italy].

Fifty-five patients, 10 to 66 years of age, with tuberculous meningitis were treated in a hospital in Ancona, Italy, from 1947 to 1957. The patients, according to the treatment given, were divided into 3 groups. The first group consisted of 28 patients, seen between 1947 and 1951, who were treated with streptomycin given intramuscularly and intraspinally; 6 of these patients recovered. The second group consisted of 12 patients, seen between 1952 and 1954, who were treated with the same drug as the patients of the first group, with the addition of isoniazid; 8 of these patients recovered. The third group consisted of 15 patients, seen between 1955 and 1957, who were treated with the same drugs as the patients of the first and second groups, with the addition of cortisone and aminosalicylic acid given intravenously; 14 of these patients recovered. None of the 28 patients who recovered permanently presented late side-effects, owing to treatment on observation 1 or 2 years after the end of the initial treatment. At these follow-up examinations, however, 2 patients presented spastic paresis and 1 a mild Jackson's syndrome with electroencephalographic focal signs. No relapses occurred after treatment in patients of the first and second groups; 2 early relapses occurred in patients of the third group, but they recovered after further treatment.

The authors believe that a combination of streptomycin, isoniazid, cortisone, and aminosalicylic acid represents today the best treatment for adults with tuberculous meningitis. Such treatment is useful in avoiding the risk of late intolerance or resistance to isoniazid, which might cause a relapse of meningeal symptoms or affect unfavorably the course of the disease, as occurred in the one patient of the third group who died. Moreover, the authors believe that aminosalicylic acid given intravenously in large quantities is especially useful in the initial hematogenous or bacillogenous stage of tuberculous meningitis.

Effects of Delayed Anticoagulant Therapy on Experimental Cerebral Infarcts. A. F. Peterman, K. G. Wakim, G. P. Sayre and others. J. Neuropath. & Exper. Neurol. 18:263-269 (April) 1959 [New York].

Although anticoagulant therapy has been used with some success in the treatment of certain types of cerebrovascular disease, a great deal of uncertainty exists about the effects of such treatment on completed cerebral infarcts. Several methods have been described by which cerebral infarcts can be produced in dogs. Since it has been shown that a cerebral infarct undergoes its most distinctive histological change by the fourth day, it was decided to start anticoagulant therapy on the third day after the production of cerebral infarction, aiming at the establishment of a reduction of prothrombin activity to the therapeutic range by the fourth day after infarction. Homologous blood clots were used to produce intracranial arterial occlusion, because this method causes cerebral infarction in the majority of animals associated with a relatively low mortality rate; also, such infarcts resemble embolic infarcts found in humans. Approximately 48 hours prior to operation, 5 ml. of blood was withdrawn from each dog and allowed to clot and stand at room temperature in a sterile test tube. Cerebral infarcts then were produced by injection of these homologous blood clots into the internal carotid artery via the common carotid artery exposed through an incision in the neck. In the animals in which a satisfactory embolic lesion was produced, the signs and symptoms of cerebral infarction were evident when the animals recovered from anesthesia. Only those dogs which showed definite signs of cerebral infarction, which survived for 3 days after the procedure, and which were otherwise in good health were included in this study.

A total of 24 dogs with experimentally produced cerebral infarcts were given anticoagulants, beginning on the third day after the induction of infarction, and they continued to receive the drugs for 9 to 15 days thereafter, with a mean prothrombin activity of 21% of normal. A group of 23 dogs with similar infarcts were not treated and served as controls. No significant difference was noted in the size of the infarct between the dogs receiving anticoagulants and the control dogs, and the clinical course of the dogs which survived the period of study was the same in each group. The homologous blood-clot embolus that was injected to produce the infarct was located proximal to the infarct in 38 dogs, and thrombosed arteries were found within the infarcts in 50% of all the dogs, whether or not treated with anticoagulants. No correlation as to the amount of hemorrhage was noted between the gross and the histological appearance of the infarcts. Dogs treated with anticoagulants had cerebral infarcts that were more hemorrhagic than those of the controls, and the mortality rate was higher in the treated dogs.

Perinatal Infections of the Central Nervous System. A. Wolf and D. Cowen. J. Neuropath. & Exper. Neurol. 18:191-243 (April) 1959 [New York].

The authors review the extensive literature on perinatal infections of the central nervous system, pointing out that the findings of Gregg in maternal rubella stimulated a search for other infections which might lead to similar results. A variety of congenital defects have been described in infants born to mothers who during pregnancy had mumps, measles, chickenpox, herpes zoster infection, scarlet fever, or infectious mononucleosis. A cause and effect relationship has not been firmly established in all of these, and there is not sufficient evidence that the infective agent entered and directly injured the nervous system. Prospective studies by several investigators demonstrated that the possibility of a congenital malformation occurring in the offspring of a woman suffering from an infection in the first trimester of pregnancy is not nearly as great as was at first feared.

The authors discuss spirochetal, protozoan, viral, and bacterial infections of the nervous system which occur in the perinatal period. These include congenital syphilis, toxoplasmosis, cytomegalic inclusion disease, herpes simplex infection, equine encephalomyelitis, and the bacterial meningitides and meningoencephalitides. Commenting on perinatal syphilis of the central nervous system, the authors conclude that congenital syphilis appears to be a diminishing problem as an infection of the neonatal nervous system due to the increasing efficacy of treatment of this infection. They present detailed histories of 2 patients with congenital toxoplasmosis and of 1 with cytomegalic inclusion disease, as well as 2 probable instances of herpes simplex infection. They conclude that, in spite of the great number of infective agents which may enter and damage the central nervous system in the perinatal period, infection must still be considered one of the less common causes of pathological changes in the brain at this time of life.

Delirium Tremens and Acute Liver Damage. G. Lundquist, E. Nettelbladt and H. Reichard. Nord. med. 61:433-436 (March 12) 1959 (In Swedish) [Stockholm].

Determinations of glutamic oxalacetic transaminase (GO-T) and ornithine carbamyl transferase (OC-T) in the serum were used as a test of acute liver damage in 32 cases of delirium tremens and in 10 of chronic alcoholism. Determinations of bilirubin and thymol turbidity were also made. Increased serum bilirubin was seen in only 10% of the cases of delirium tremens. Most of the patients with delirium tremens had increased serum levels of both GO-T and OC-T, presumably due to acute liver damage. Since not all these patients showed signs of acute liver damage, the latter cannot be the primary cause of delirium tremens. There was moderate to marked increase in GO-T and OC-T values in chronic alcoholics who had ingested large amounts of alcohol shortly before admission.

Studies on Spontaneous Primary Encephalitides in the Monkey: I. A Polio-Encephalitis with Predilection for the Brain Stem in the Baboon (Papio Hamadryas). L. van Bogaert. J. Neuropath. & Exper. Neurol. 18:294-305 (April) 1959 [New York].

The author observed in 3 monkeys disease similar to the human primary polioencephalitides which chiefly affect the brain stem. His first observation was made on a 2-year-old male baboon (Papio hamadryas) in 1937. In 1940 and in 1946 he was able to study 2 other baboons with disorders of this type. In the first baboon there developed simultaneously with diarrhea and fever attacks of extremely violent generalized epilepsy, with occasional Jacksonian components, bilateral hemiparesis, a postural tremor, and a left peripheral facial paralysis. In the second baboon a neurological syndrome developed suddenly, which included epilepsy, cerebellar tremor of the entire body, myoclonic jerks, transient torticollis, palsies of the 3rd, 5th, 7th, 9th, and 10th cranial nerves, and a terminal hemiplegia. The course of the illness was 17 days. The third baboon suddenly showed anger and excitement, with myoclonus, generalized tremor which was slight at rest and increased by movement, some choreoathetoid movements, paralysis of the 7th and 9th cranial nerves, and finally severe generalized hypotonia. The paroxysms of aggressiveness were followed by a period of relaxation, which was succeeded by a postictal stupor. The animal refused to eat or drink.

The pathological picture in the first 2 animals was that of a severe encephalitis of the entire brain stem, spreading anteriorly to the hypothalamus and the septal nuclei, and laterally to the claustrum. The cord presented perivascular and nodular infiltrations in the posterior more than in the anterior gray matter, with moderate involvement of the white columns. The author concludes that a meningopolioencephalitis exists in baboons which has a predilection for the brain stem. The disease has an acute and fatal course. The localization and characteristics of the disease process are reminiscent of those seen in Borna disease (encephalitis of horses, cattle, and sheep caused by a virus) and rabies. Clinically, the disease is characterized by sudden behavior disturbance (anxiety, aggressiveness, fits of temper), paretic disorders, myoclonus, postural tremor, at times transient choreoathetoid movements, cranial nerve palsies, and epileptic attacks. The fundi are normal. Modifications of the cerebrospinal fluid could not be determined. This type of meningoencephalitis has a specific clinicopathological character.

GYNECOLOGY & OBSTETRICS

Combined Treatment of Carcinoma of the Ovary. D. Buttenberg and H. Lau. Geburtsh. u. Frauenh. 19:308-325 (April) 1959 (In German) [Stuttgart, Germany].

The authors describe the method of combined treatment of carcinoma of the ovary, which has been practiced since 1954 at the gynecologic clinic of the University in Heidelberg, Germany. It consists of (1) excision of both ovaries without removal of the uterus, or, if this proves impossible, removal of the bulk of the tumor but without attempting to eradicate radically all carcinomatous tissue, since such an attempt may expose the patient to complications in the course of the surgical intervention and postoperatively; (2) repeated intra-abdominal instillation of single doses of 120 mc. of radiogold (Au^{198}), the first dose being given immediately after the operation and its administration being repeated at least once at an interval of 2 or 3 months; (3) intrauterine application of radiocobalt (Co^{60}) pearls, with a maximum load of 4,000 r placed on the bladder and the rectum; (4) percutaneous depth roentgen irradiation with use of a grid and one field, each over the abdomen and the back, with a surface dose of 6,000 r, or telecobalt therapy with doses of 4,000 to 5,000 r; and (5) continuous therapy with large doses of androgens combined with administration of prednisone.

With this treatment the survival time of 24 women with incurable carcinoma of the ovaries could be prolonged by an average of 3 months, compared with that of a similar group of 29 patients who had been treated between 1945 and 1950. In view of the highly unfavorable prognosis of carcinoma of the ovaries, this prolongation of the survival time, although it is short, is of some value, particularly since the patients had a subjective feeling of well-being. The use of cytostatic agents is rejected because of the additional risk of damage to the leukopoietic system. Hypophysectomy is advocated as a supplementary measure to hormone treatment.

Ferrodynamics During Pregnancy. R. G. Holly and W. J. Ground. Am. J. Obst. & Gynec. 77:731-742 (April) 1959 [St. Louis].

Storage iron estimates were made on 19 pregnant women, since it was found that iron depots are reduced in the majority of women at the onset of pregnancy. The demands for iron by the fetus and by the mother for extra hemoglobin synthesis are in excess of that which can be supplied by diet alone. Storage iron is "available iron" and can be mobilized for the fetal requirement or for maternal hemoglobin production. Eleven of the 12 patients studied early in pregnancy were shown to have diminished or depleted iron stores. It is significant that the patients with iron stores had hemoglobin values above 11.4 Gm. per 100 cc. These observations confirm the impression based on clinical studies that the hemoglobin level will remain normal if an iron supplement is available and provided that bone marrow function is normal. The presence of a normal hemoglobin level does not mean, though, that there is storage iron. One patient with a hemoglobin level of 11.4 Gm. per 100 cc. had no visible storage iron.

Radioiron (Fe^{59}) studies were performed on 7 patients, 3 of whom exhibited deficiency anemia caused by pregnancy. Plasma iron turnover rates were found to be decreased during pregnancy. A similar reduction in the erythrocyte iron turnover rate was observed. These findings could be explained on the basis of iron deficiency. A theory postulating a retarded erythrocyte production rate was advanced. It was based on the low erythrocyte iron turnover rate, on the retarded erythrocyte utilization of Fe^{59}, and on the relatively high liver counts obtained by surface scanning. Iron deficiency is the commonest cause of pregnancy anemia. There is apparently some degree of bone marrow suppression in association with pregnancy.

Ethical, Religious and Legal Aspects of Artificial Insemination as Viewed by a Gynecologist. L. Sbrocca. Minerva ginec. 11:158-165 (Feb. 28) 1959 (In Italian) [Turin, Italy].

Artificial insemination was condemned by the Roman Catholic church in 1897, and this position was reaffirmed by the Jesuit priest, F. Hürth, in an article published in 1946. Hürth left the discussion open for further study, because it did not involve the domain of either faith or dogma. Theologians have argued that only natural copulation, being an uninterrupted action in the process of procreation, is admissible. The author contends that the mechanism of natural coitus should not be overemphasized, because its object is procreation, but the motive force is sensual pleasure. Moreover, coitus has no bearing on the act of creating, which process is independent of the will of either the man or the woman. The author believes that moral principles cannot be offended if the result of conception, fructus ventris, is obtained either through natural coitus or by the aid of a physician through artificial insemination. Artificial insemination is thus viewed as a corrective measure for a defect of natural coitus and is justifiable only for the transmission of semen of the husband into his wife. Artificial insemination through a donor violates ethical-religious principles, and the use of such impregnation by an unmarried women is an even greater offense.

Children born by the aid of artificial insemination between husband and wife are legitimate according to the interpretation of Italian law. Recently a lower court in Italy had to decide on the first penal case of artificial insemination in that country. In the absence of an explicit provision, the court ruled that the defendant, a legally separated woman, who gave birth to a child through the semen of an anonymous donor, was not an adulteress and thus that her child was not born out of wedlock. The author concludes that artificial insemination is becoming a pressing problem, which requires passage of specific guiding rules by both lay and ecclesiastical authorities.

Fetal Mortality and Prematurity with Repeat Abdominal Delivery. A. W. Diddle, V. Gibbs and S. Lambeth. Am. J. Obst. & Gynec. 77:719-730 (April) 1959 [St. Louis].

It has been shown that fetal mortality is greater with cesarean section than with vaginal delivery. The greater loss is generally attributed to the obstetric complication leading to the hysterotomy and not to the operative procedure. Fetal salvage, even with repeat cesarean section, may, however, be less favorable than with the average delivery, since babies born in this circumstance are not infrequently premature. In this study of fetal mortality with repeat cesarean section, it was found that 11% of the babies born by repeat cesarean section or following uterine rupture were premature. This was a higher percentage than for the average vaginal delivery. More than half of the babies born by repeat abdominal delivery died either of prematurity after elective cesarean section or of anoxia in association with a rupture of the uterus. A decrease in the incidence of premature infants delivered by elective repeat cesarean section and in the number of uterine ruptures accounted for a fall in the fetal mortality in the second half of the study as compared with the first half. It appears that the danger of uterine rupture from waiting until the baby was at term was offset by the risk of elective delivery of a premature baby.

Elective repeat cesarean section is nearly as safe for the baby as vaginal delivery in some hospitals. This safety is the result of careful timing of the operation according to the maturity of the fetus. The menstrual age was found to be unreliable as a measure for determining when a pregnancy was at term. Infants delivered by elective repeat cesarean section were seldom premature if the cervix was effaced, if the crown–rump length of the fetus was at least 25 cm., as determined by palpation, and if the ossification centers were visible in the fetal epiphyses of the knees, as ascertained by roentgenographic study. Experience indicates that it is usually advisable to defer repeat cesarean section until the onset of spontaneous labor if there is doubt as to the maturity of the baby.

Normal Pregnancy and Delivery in Female Pseudohermaphroditism. F. Gans and J. Ser. Acta endocrinol. 30:424-434 (March) 1959 (In English) [Copenhagen].

The authors present what they believe to be the first report of the delivery of a healthy child of a female pseudohermaphrodite, after cortisone therapy over several years and after plastic operation. When first examined by the authors in 1953, the patient was 16 years old and complained of amenorrhea and of hair on the body and face. Her mother had suffered during pregnancy from a hypophyseal tumor and had received x-ray therapy, but the girl's development during childhood had been normal. At the time of observation the patient's voice was remarkably low. There was hirsutism on the face, extremities, abdomen, and, to a less degree, the upper part of the body. The breasts were not developed. The clitoris was about 4 cm. long. The labia majora were well developed; the labia minora were absent; and no vaginal aperture was found. Rectal examination revealed a small uterus, and both ovaries were present. The psychic attitude of the patient was feminine. Clinical and laboratory findings justified the diagnosis of female pseudohermaphroditism (congenital adrenal hyperplasia). Cortisone therapy was started in September, 1953, with daily injections of 100 mg. of the drug. About 8 months after the onset of this therapy menstruation began, and from then on it occurred in almost regular monthly cycles.

In September, 1956, the patient requested an operation for correction of her genital malformation. At this time she received injections of 100 mg. of cortisone every 4th day. Cytourethrography revealed that the orifice of the urethra was at its normal site. An x-ray picture of the pelvic outlet (after injection of a contrast medium into the sinus urogenitalis) showed a vagina, distally narrowing into a small canal; the proximal vaginal filling showed an appendage obviously corresponding to the filled cervical canal. An amputation of the enlarged clitoris was performed, and the sinus urogenitalis was incised. The vagina, lying behind, was partly freed from the underlying tissue, broadened by means of longitudinal incision, and sutured to the skin. Dilatation therapy was started after the operation and was continued at home.

Examination in July, 1957, revealed that the patient was 2 months pregnant. She was given the usual dose of cortisone and felt well during the entire pregnancy. Except for cortisone, the patient received no hormonal treatment of any kind. Despite, or maybe because of this, the breasts developed normally, the menses appeared, and hirsutism diminished. Theoretically it is conceivable that the administration of additional quantities of estrogens, as well as cortisone, might have produced adverse effects because of inhibition of follicle-stimulating hormone production by the hypophysis. The course of events in this case is in favor of the exclusive administration of cortisone. The patient received cortisone for 4½ years and during her entire pregnancy without any perceptible disadvantages. The regular control of electrolytes showed no significant deviation from the normal. The weight remained unchanged, and during the whole treatment the state of the patient's health was better than ever before.

PEDIATRICS

Studies in Sickle-Cell Anemia: XII. Further Studies on Hepatic Function in Sickle-Cell Anemia. A. D. Ferguson and R. B. Scott. A. M. A. J. Dis. Child. 97:418-425 (April) 1959 [Chicago].

Despite clinical evidence of involvement of the liver in children with sickle-cell anemia, difficulty is usually observed in quantitating hepatic dysfunction by the traditional liver function tests, such as serum bilirubin, van den Bergh, alkaline phosphatase, cephalin flocculation, total protein, and serum glutamic oxalacetic transaminase. In an attempt to obtain additional evidence of impaired liver metabolism by the use of some of the newer laboratory procedures, serum protein separation by filter-paper electrophoresis was carried out on 28 children, between the ages of 10 months and 16 years; 51 blood ammonia determinations were made on 26 children, ranging in age from 2 to 12 years; and urinary amino-acid analyses were performed on 5 children, between 4 and 10 years of age, all with sickle-cell anemia. These newer procedures proved to be similar to the traditional liver function tests in that they were not conclusively diagnostic. However, as a battery they were at times helpful in supplying additional confirmatory evidence of hepatic damage in young children with sickle-cell anemia, in whom the correlation between liver damage and the results or response obtained from the usual function tests is less reliable than in older persons.

A needle biopsy specimen of the liver was obtained from a 5-year-old boy with sickle-cell anemia, who was hospitalized during a crisis associated with a complicating pneumonia. Microscopic examination of the specimen showed that the sinusoids were dilated and plugged with sickled cells. In some areas the sinusoids were practically occluded by the stagnation of sickled and hemolyzed erythrocytes. The liver cord cells were swollen, granular, and pale, indicating early degenerative change. Biopsy of the liver is not indicated as a routine procedure in all children with sickle-cell anemia and should not be attempted by unqualified persons. Occasionally, microscopic study of hepatic tissue obtained by needle biopsy may be helpful in establishing a definite diagnosis in children in whom chemical tests are negative or equivocal in the presence of persistent spectacular enlargement of the liver, which cannot be readily explained by other causes.

Long-Term Use of Prednisone and Prednisolone in Juvenile Rheumatoid Arthritis: A Report of Fifteen Cases. E. E. Harnagel. A. M. A. J. Dis. Child. 97:426-431 (April) 1959 [Chicago].

Seven girls and 3 boys, with rheumatoid arthritis, and 4 boys and 1 girl, with rheumatoid spondylitis, were treated with prednisone and prednisolone for periods ranging from 8 to 24 months. The average age of the 15 patients was 14.4 years, and the average daily maintenance dose varied from less than 5 to 20 mg. These doses, calculated on a per pound basis, were in excess of those usually given to adults with rheumatoid arthritis. Prednisone and prednisolone were used interchangeably. Treatment with these steroids was reserved principally for those patients whose condition had not been satisfactorily controlled with acetylsalicylic acid and/or cortisone. Although 12 (80%) of the 15 patients obtained satisfactory relief from pain and stiffness, only 3 (20%) had complete remission of the disease during the period of treatment, and 6 had major or minor improvement. Six patients (40%) were unimproved or became worse, and in 4 of these progressive articular destruction was observed. A total of 28 untoward reactions, such as "moon face," acne, mild psychic changes, and striae, were observed; these were largely of minor importance and did not require a reduction of dose or withdrawal of the steroid agent. The most formidable complication was diabetes mellitus, which developed in one patient while he was receiving prednisone but which went into remission while the hormonal therapy was continued. The administration of adrenal cortical steroids to children and adolescents with rheumatoid arthritis should be limited to severe progressive cases.

Clinical Features of Infection with Hemadsorption Viruses. R. H. Parrott, A. Vargosko, A. Luckey and others. New England J. Med. 260:731-738 (April 9) 1959 [Boston].

A previous report described the recovery of 2 new myxoviruses, hemadsorption viruses, types 1 and 2, which were isolated in October, 1957, from the oropharynx of children, with acute respiratory disease. The authors report clinical data on 52 boys and 40 girls, between the ages of 2 weeks and 9 years, with respiratory tract illnesses who attended the Children's Hospital in Washington, D. C., between October, 1957, and May, 1958. Of these 92 patients, 42 had infection due to hemadsorption virus, type 1, and 50 had infection due to hemadsorption virus, type 2. Thirty-three of the group of 42 patients and 29 of the group of 50 patients required hospitalization for severe illness, such as bronchopneumonia, bronchiolitis, croup syndrome, and severe pharyngitis. The remaining 9 patients of the group with type 1 virus infection and the remaining 21 patients of the group with type 2 virus infection had minor respiratory tract illnesses and were seen during visits to the outpatient department. The more severely ill patients had respiratory distress (type 1 virus infection) or cough of croup type (type 2 virus infection). Cough, rhinorrhea, and sore throat were the major symptoms in the outpatients. Pharyngeal erythema and rhinitis were the major physical signs, but the patients who became more severely ill showed dyspnea and had abnormal lung findings, such as rhonchi and rales (associated with type 1 virus infection) or signs of laryngeal obstruction (associated with type 2 virus infection). These observations suggest that the occurrence of pneumonia or croup represents a progression from the less severe type of illness. No distinct clinical features of hemadsorption virus infections were observed to enable the clinician to make the diagnosis without the aid of a virus laboratory.

Poliomyelitis Virus Neutralizing Antibodies After Salk-Vaccination in Kindergarten and School Children: Studies on Capillary Blood with a Microdye Test. M. Just, G. Ritzel and E. Berger. Helvet. med. acta 26:65-69 (March) 1959 (In German) [Basel, Switzerland].

About 20,000 children of kindergarten and school age of Basel, Switzerland, were vaccinated against poliomyelitis in 1957. The vaccinations were carried out with Salk vaccine of American origin. The children were given 3 subcutaneous injections of 1 cc. of vaccine into the upper arm. The interval between the first 2 injections was 4 weeks and between the second and third, 6½ months. The authors describe studies carried out to ascertain whether the children had an adequate antibody level against poliomyelitis virus after the vaccination. The capillary blood was examined for virus neutralizing antibodies with the aid of a microdye test from 2 to 4 weeks after the third injection of Salk vaccine. The test used had been described by Löffler and Vogt in 1957. A macrodye test with blood obtained by venous puncture was used in some of the children as a control, and the 2 tests were found to produce identical results. Tests were made on 3 groups, of about 100 children each, a total of 281: (1) children, 4 and 5 years old; (2) children, 9 and 10 years old; and (3) children, of 13 and 14. Antibody formation was best against type 2 and poorest against type 3 poliomyelitis virus. Electrophoretic analysis of the serum proteins of children who had an insufficient increase in virus neutralizing antibodies against poliomyelitis virus after vaccination revealed no difference in comparison with the serum proteins of normal controls.

A Fatal Granulomatous Disease of Childhood: The Clinical, Pathological, and Laboratory Features of a New Syndrome. R. A. Bridges, H. Berendes and R. A. Good. A. M. A. J. Dis. Child. 97:387-408 (April) 1959 [Chicago].

The authors report on 4 boys, between the ages of 7 months and 5 years, who were referred to the department of pediatrics of the University of Minnesota Hospitals in Minneapolis with a syndrome consisting of chronic suppurative lymphadenitis, hepatosplenomegaly, pulmonary infiltrations, and an eczematoid dermatitis about the eyes, nose, and mouth. These manifestations proved to be the result of a generalized granulomatous process and were associated with a prominent hypergammaglobulinemia. All 4 patients died, and autopsy performed on 3 revealed generalized involvement of the reticuloendothelial system, including every group of lymph nodes throughout the body and, in addition, the liver, spleen, lung, and skin. The clinical syndrome presented by these children closely resembled tuberculous cervical adenitis. From the family history of one of the patients, it appeared that 2 maternal uncles had died, at the ages of 7 and 8 months, with what, by the description given by the patient's mother, may have been the same disease as that of the patient. The maternal grandfather was also supposed to have had the same syndrome. These findings suggest that the disease may occur in male members over several generations. Though periods of symptomatic improvement occurred even after the development of pulmonary lesions, these would appear to mark the terminal phase of the disease. At this time the previously suppurative adenopathy, which represented the first manifestation of the disease, became quiescent, and the debilitating systemic manifestations assumed the most prominent role, leading to death within a year of this event.

The various laboratory examinations, including determinations of gamma globulin concentration and immunological capacity, skin tests performed with antigens prepared from pathological material obtained from one of the patients, and white blood cell function tests, as well as the findings at autopsy, made it possible to differentiate this new syndrome from recognized forms of infectious and noninfectious disease producing granulomatous processes in childhood. The tests did not make it possible, though, to arrive at an etiological characterization of the syndrome, which appears to be a distinct entity, the causation of which is yet to be determined. Extensive empirical efforts at treatment have been without effect on the relentless progression that would seem to be the most characteristic feature of this syndrome.

UROLOGY

Treatment of Vesical and Prostatic Carcinoma with Atomic Medicine. C. F. Rusche and H. L. Jaffe. J. Internat. Coll. Surgeons 31:305-314 (March) 1959 [Chicago].

The authors obtained improved results in the treatment of patients with carcinoma of the bladder or of the prostate by using a combination of surgical treatment, injection of radioactive colloidal chromic phosphate, and external irradiation with a radiocobalt (Co^{60}) bomb. Although this combined treatment achieves only palliative benefit in advanced stages of the disease, some patients have achieved arrest for more than 4 years. In addition to high tumor doses being administered without untoward effects, this combination of isotopic and Co^{60} bomb therapy enables the therapist to direct the treatment accurately to the tissues involved. There is minimal damage to the surrounding normal tissue, and secondary contracture of the bladder is absent.

In carcinoma of the bladder, clinical classification, based on gross appearance and extent, is essential for deciding on the best treatment. If stage 1 bladder tumors are too extensive for segmental resection or if the trigone or outlet is involved, the authors prefer fulguration and interstitial implantation of radioactive colloidal chromic phosphate. (The isotope, which is prepared from radiophosphorus [P^{32}], has a half-life of 14.3 days.) This is followed by a full course of external rotation Co^{60} therapy if there is subsequent recurrence of the tumor.

For stage 2 tumors, segmental resection is done when there is a single infiltrating tumor which proves to be resectable. Only when subsequent microscopic examination reveals that an inadequate amount of surrounding normal mucosa has been removed, or when there is evidence of local recurrence, do the authors employ postoperative Co^{60} bomb therapy. If the tumor is nonresectable, they remove the bulk of it electrosurgically and fulgurate its base. Then they inject the isotope or radon seeds. The Co^{60} bomb is used only if there is residual disease after 3 months. When cystoscopic examination reveals multiple infiltrating tumors, the authors perform open operation and fulgurate each tumor to its base after removing the bulk of it electrosurgically. Radon seeds or the isotopes are injected at the tumor base, and Co^{60} bomb therapy is used after 3 months if the inspection biopsy is positive.

In stage 3 tumors, when operation reveals that the neoplasm is infiltrating and extending through the bladder wall into the perivesical fat or into the regional lymph nodes, the authors remove the bulk of the tumor electrosurgically and fulgurate its base. They also remove a lymph node for biopsy. In case of lymph node metastases, intensive Co^{60} bomb therapy is given, but interstitial irradiation is not used. If there is local recurrence after Co^{60} bomb treatment, a "second look" operation and interstitial isotope injection are carried out. Patients with stage 4 lesions (distant metastases) are given palliative Co^{60} therapy. Of 36 patients with carcinoma of the bladder, who were treated by this technique and followed for almost 3 years, 24 are alive, and 12 are dead. Of the surviving patients, 15 had good results, 3 fair results, and 3 poor results, while 3 have been treated recently. Of the 12 deceased patients, 1 had a good result, 2 fair results, and 6 poor results; 3 did not complete the treatment.

In carcinoma of the prostate, radical perineal prostatectomy is the treatment of choice for the patient with an operable lesion; the combined technique of isotopic-surgical therapy and Co^{60} irradiation is indicated only for the one with inoperable prostatic carcinoma. The authors previously reported their technique and results with radioactive colloidal chromic phosphate in the treatment of advanced prostatic carcinoma. Although they were impressed with the results from a palliative standpoint, there were some patients who required more than local injection treatment because of further tumor growth. Instead of giving more injections of chromic phosphate at 3-to-4-month intervals, the authors resorted to Co^{60} bomb rotation therapy, and of the 15 patients who received either the combined treatment or the Co^{60} therapy alone, at least two-thirds obtained worthwhile results.

Spontaneous Rupture of the Bladder. J. R. G. Bastable, L. R. De Jode and R. P. Warren. Brit. J. Urol. 31:78-86 (March) 1959 [Edinburgh].

The authors include under the term "spontaneous rupture of the bladder" all cases of sudden vesical rupture into the peritoneal cavity or the pelvic cellular tissue when there was no injury. This definition excludes vesical fistulas into the vagina and colon, or through suprapubic scars; rupture following instrumentation, such as cystoscopy, cystodiathermy, or litholapaxy; rupture caused by the introduction of foreign bodies or by attempts to cause abortion; extension of uterine or vaginal tears during parturition; and rupture following ulceration due to indwelling urethral catheters. Four patients with spontaneous rupture of the bladder were seen at the London Hospital during the last few months, and a search through the hospital records since 1900 revealed 2 further cases. The histories of these 6 patients are described, together with a review of 66 cases collected from the literature in the last 25 years.

These 72 cases included 66 of intraperitoneal rupture, 5 of extraperitoneal rupture, and 1 of combined intraperitoneal and extraperitoneal rupture. All 5 patients with extraperitoneal rupture were men. Two of these patients had stricture, one an enlarged prostate, and one a vesical papilloma with obstruction of the internal meatus; 3 of them recovered, and one died under the anesthetic. The 5th case of extraperitoneal rupture was due to tuberculosis, and the patient died. Of the 66 cases of intraperitoneal rupture, 14 occurred in women and the remainder in men. The youngest patient was 21 years old. All 3 patients with recurrent rupture were men. With regard to causation, the intraperitoneal ruptures fall into 2 main groups, depending on whether the rupture was due to a lesion of the bladder wall or was caused by overdistention of the bladder. There were 28 patients with lesions of the bladder; these included 9 with tuberculosis, 5 with carcinoma, 7 with cystitis, 6 with scars, and 1 with "lipomatosis." The 38 patients in whom retention was the cause of rupture included 4 with neurological disorders, such as tabes dorsalis or paraplegia, 19 with various forms of urinary obstruction, and 15 in whom the rupture was considered to be secondary to a reflex retention. Rupture usually occurred through the vault of the bladder and was small in lesions of the bladder wall.

Diagnosis in spontaneous rupture depends on a history of pain and disturbance of micturition and the signs of peritonitis. Catheterization and withdrawal of blood-stained urine confirm the diagnosis, but occasionally the urine is clear. The mortality in the series presented was 47% and has not fallen during the last 25 years. Carcinoma, tuberculosis, and enlarged prostate accounted for two-thirds of the deaths.

Family with Cystic Kidneys and Cystic Liver in Several Generations. A. L. Ørbeck. Tidsskr. norske laegefor. 79:193-195 (Feb. 15) 1959 (In Norwegian) [Oslo].

Twenty-four cases of cystic kidney in one family, both sexes equally represented, are reported. In 4 cases there was simultaneous cystic liver. The symptomatology was fairly uniform with acute and more or less marked hematuria, at the onset or later in the course, and proteinuria, possibly with infection of the urinary tract and pyuria, hypertension and uremia, together with symptoms as the result of growth of the tumor. The clinical course of the disease seems to be fairly uniform and gradually leads to death from uremia, if expansion of the renal tumor or intercurrent diseases do not advance the course. Transmission is apparently abiotrophic dominant. The disease may be latent for many years or manifest itself late in a tissue which was hitherto normal.

INDUSTRIAL MEDICINE

Chelating Agents in the Therapy of Beryllium Poisoning. R. Cash, R. I. Shapiro, S. H. Levy and S. M. Hopkins. New England J. Med. 260:683-686 (April 2) 1959 [Boston].

The authors studied the effect of edathamil (ethylenediaminetetraacetic acid [EDTA]) on the renal excretion of beryllium in 2 patients with proved beryllium pneumoconiosis. The causative agent was found by spectrographic analysis of pulmonary parenchyma obtained by lung biopsy. Both patients had been exposed to beryllium for varying periods during their employment. Both had moderate to marked pulmonary insufficiency. Trisodium edathamil was slowly infused intravenously in concentrations of 0.5 to 1.0 Gm. dissolved in 1,000 cc. of 5% dextrose in water. The drug was administered intermittently over a 3-day period. The first patient received a total dose of 2.8 Gm., and the second patient a total dose of 3 Gm. during this period. On the 4th day of therapy the second patient received a total dose of 3 Gm. of calcium edathamil. Twenty-four-hour or 48-hour samples of urine were collected and analyzed for beryllium content with the aid of a mass spectrograph.

The results showed that edathamil therapy induced a definite increase in the renal excretion of beryllium. This increase was observed in the total daily excretion as well as in the concentration per liter of urine. Calcium edathamil was found to have a similar effect as trisodium edathamil. Edathamil, a polyamino carboxylic acid, forms a water-soluble, relatively un-ionizing chelate with polyvalent cations and has been shown to cause marked increase in the excretion of heavy metals, without the usual toxicity associated with reaction of the metal ion with body tissues. It is suggested that long-term intermittent therapy with a chelating agent such as edathamil may so deplete the body stores of baryllium ion that the clinical course or progress of the disease may be favorably affected.

Talc Pneumoconiosis. A. O. Seeler, J. S. Gryboski and H. E. MacMahon. A. M. A. Arch. Indust. Health 19:392-402 (April) 1959 [Chicago].

The authors report clinical and postmortem observations on 2 men, aged 73 and 70 years, with talc pneumoconiosis who worked for about 25 years as "lay-up" men in a factory manufacturing rubber-coated cable. Their work was to stand near the machines that coated the cables with rubber and coil the freshly coated cable into pans that were filled with talc. It was the practice to shovel a layer of talc into each pan and then coil the wire on this layer. As soon as a coil of wire was laid in the pan, talc was shoveled on in preparation for the next layer of cable. Although dust counts were not available for the period of years that the men worked with talc, the work created a great deal of talc dust, and there was no ventilation, so dust counts would have been very high. The autopsy findings in both patients were similar and showed the pattern of a chronic, crippling, progressive disease of the lungs by scar tissue, injury, and destruction of blood vessels, dilatation of bronchi and alveoli, and slighter degrees of fibrosis and atelectasis throughout the rest of the lung. The presence of large quantities of doubly refractile needle-shaped particles in the area of fibrosis would appear to be the causative factor responsible for this particular form of pneumoconiosis. Although the lungs of both patients showed extensive fibrosis, this did not show a specific pattern that might be of diagnostic value. In neither case were the classic laminated nodules observed.

THERAPEUTICS

Placebos in the Evaluation of Treatment in Rheumatic Diseases. E. F. Traut and E. W. Passarelli. Illinois M. J. 115:181-183 (April) 1959 [Chicago].

Four hundred twenty-six patients with various rheumatic diseases, such as rheumatoid arthritis, degenerative arthritis, psoriatic arthritis, and shoulder syndromes, were given placebo tablets for 4 weeks or less. Those patients who did not respond, or ceased to respond, to placebos in tablet form were given hypodermic injections of 1 cc. of an isotonic solution of sodium chloride at weekly visits for 4 weeks or less. Of the 426 patients, 226 were relieved for significant periods by placebo tablets. Of the remaining 200 patients, 114 were relieved by injections of saline solution. Thus, 340 of the 426 patients responded favorably to placebo therapy.

Fluctuation of the clinical manifestations of the chronic forms of these rheumatic diseases is axiomatic. Their principal symptom is pain, a function of the cerebrum, which is influenced by many factors. In all chronic illnesses, including rheumatic disorders, the psyche plays an important role, affecting favorably or unfavorably the course of the disease, even deciding its outcome or its inception. Thus, the use of placebo medications seems justified. The number of rheumatic patients found to benefit from such medications is about the same as the number favorably influenced by any or all the methods of therapy reported in other studies. This was evident in sufficient degree and in a large enough group of patients to justify the continuance of placebo therapy. The number of patients benefited did not seem to be essentially altered by resorting to salicylates or even to cortisone.

Current Status of Amphotericin B in the Treatment of the Systemic Fungus Infections. V. D. Newcomer, T. H. Sternberg, E. T. Wright and R. M. Reisner. J. Chron. Dis. 9:353-374 (April) 1959 [St. Louis].

Promising laboratory studies with Amphotericin B, a new polyene antifungal antibiotic, prompted the authors to report on 22 patients with various systemic mycoses, who were treated with that drug either under direct observation or in cooperation with other physicians. The ages of the patients ranged from 2½ to 62 years. They were followed up after treatment for periods varying from 5 months to 2 years. Fourteen of the 22 patients had coccidioidomycosis; 5, cryptococcosis; 1, North American blastomycosis; 1, candidiasis; and 1, mycetoma. Five of the 14 patients with coccidioidomycosis had coccidioidal meningitis. Three of these 5 patients improved clinically, but the titer of their complement-fixation tests for coccidioidomycosis showed no essential change. Two of these patients remained clinically improved over 4-month and 5-month follow-up periods, while the third patient had a relapse 7 months after treatment. One patient was lost to follow-up, and the 5th patient died after 7 weeks of treatment. Six of the remaining 9 patients with disseminated coccidioidomycosis showed clinical evidence of improvement while under direct observation. This included an early increased feeling of well-being, improved appetite, gradual weight gain, increased strength, decreased fever, stabilization, reduction in size, or complete resolution of pulmonary infiltrates, healing of draining sinuses, and partial or complete healing of cutaneous lesions. Of the 5 patients with cryptococcic meningitis, 3 showed moderate to marked clinical improvement. The spinal fluid cultures remained negative, pleocytosis returned toward normal, and the spinal fluid sugar and hydrodynamics reverted toward normal; however, some abnormalities still existed in the spinal fluid. Two patients with cryptococcic meningitis died; one had received Amphotericin B orally in doses of 16 Gm. a day for a total period of 16 days. The drug had a beneficial effect on the patient with North American blastomycosis and on the patient with candidiasis, but the condition of the patient with mycetoma did not improve.

Results revealed that Amphotericin B is poorly absorbed from the gastrointestinal tract and that, when given orally, the drug failed in the majority of cases to influence appreciably the clinical course of any of the systemic mycoses, even when it was administered in large doses over long periods of time. However, intensive oral therapy with Amphotericin B should be given a fair trial in patients for whom intravenous therapy is not possible. The drug has been well tolerated in oral doses ranging from 8 to 12 Gm. a day, and one patient tolerated doses as high as 16 Gm. a day. The intravenous route has appeared to be the more satisfactory method of administering Amphotericin B. In the adult the optimal dosage is in the range of 0.7 to 1.4 mg. per kilogram daily over a period ranging from 2 weeks to 4 months. Evidence has indicated, though, that the drug is better tolerated and is equally effective in the same dosage level when administered on alternate days. The initial dose should be in the range of 5 to 10 mg. a day, with increments of 5 to 10 mg. depending upon the reaction of the patient. A persistent drop in the hematocrit has been observed in some patients. It is, therefore, recommended that appropriate hematological, liver-function, and renal-function studies be performed on all patients who receive prolonged treatment with Amphotericin B.

A New Antituberculous Medicament: Alpha-Ethyl-Thioisonicotinamide or 1314 Th: Experimental Bases of Its Clinical Utilization. N. Rist, Miss F. Grumbach and D. Libermann. Presse méd. 67:625-626 (March 28) 1959 (In French) [Paris].

Alpha-ethyl-thioisonicotinamide, also known as ethioniamide or 1314 Th, is as active against tubercle bacilli resistant to isoniazid as it is against normal tubercle bacilli. Its experimental activity lies between those of isoniazid and streptomycin; consequently, it can be used to replace these drugs in all cases in which the bacilli have become resistant to either or both. The appearance of isoniazid resistance can be avoided by the administration of ethioniamide and isoniazid in association. The fact that both these drugs can be given orally will make this combination easier to administer than those of isoniazid and PAS or isoniazid and streptomycin.

Laboratory studies show that resistance to ethioniamide alone develops as rapidly as resistance to isoniazid. Clinicians who wish to use ethioniamide to obtain not merely transient improvement in functional symptoms but rather definitive sterilization of the sputum should keep this danger constantly in mind and should prescribe it only in association with one, or better still two, other antituberculous drugs that are still active against the patient's bacilli. The choice of the drug or drugs to be used in such an association presupposes a thorough study of the sensitivity of the bacilli to all antituberculous drugs. Such drugs are usually given in combinations, and in vitro studies may provide an agreeable surprise by showing that the bacilli are still sensitive to one of the drugs that has already been given in a combination to which resistance has apparently developed.

The general rule that the best antituberculous drugs are poor antileprous drugs, and vice versa, does not seem to apply to ethioniamide. Early trials of isonicotinic thioamide without the ethyl group in the alpha position (3264 Th) apparently produced encouraging results, and it is reasonable to suppose that ethioniamide, which is 4 times as effective as the unmodified substance against Mycobacterium tuberculosis, will also be more effective against the bacilli responsible for leprosy (Hansen's disease).

Chlorothiazide. C. Laroche and A. Nenna. Presse méd. 67:549-551 (March 21) 1959 (In French) [Paris].

Chlorothiazide is a sulfonamide and a carbonic anhydrase inhibitor, with diuretic properties quite like those of the mercurial diuretics, except that it has no toxic effect on the renal cells. A second advantage possessed by chlorothiazide over other substances that act directly on the renal tubules is that it does not provoke acidosis or massive calcium excretion, and this makes it more manageable than acetazolamide. It comes in 0.5 Gm. tablets, to be taken by mouth, and the usual dose is from 1 to 2 Gm. daily, given in from 2 to 4 divided doses. Intravenous administration is also possible, but the results are apparently no better than when the oral route is used.

Cardiac edema provides the principal indication for chlorothiazide. The diuretic effect usually appears 2 or 3 hours after the drug is taken. The action of digitalin seems to be favored by chlorothiazide, but clinical and electrocardiographic signs of digitalis intoxication may appear rapidly. These complications can be explained by a drop in the potassium level in the blood. Digitalis should, therefore, be used in moderate doses; its effect should be closely watched; and the patient should be given from 1 to 4 Gm. of potassium chloride a day by mouth. Special care must also be taken in prescribing chlorothiazide for cardiac patients presenting signs of renal insufficiency with azotemia. Slight albuminuria and moderate hyperazotemia are not contraindications to the use of chlorothiazide; indeed, the renal signs may even improve under chlorothiazide treatment if they are related to the cardiac insufficiency, but the azotemia must be watched because it may rise rapidly. Other patients in whom chlorothiazide must be used with caution are those with cirrhosis: the results are usually mediocre, and the complications may be severe.

Chlorothiazide is effective in certain nephrotic syndromes without hyperazotemia and in edema of pregnancy, but in patients with renal insufficiency it is dangerous and does little to increase diuresis. Patients with hypertension are sometimes helped by treatment with chlorothiazide. Its hypotensive effect is very inconstant when it is used alone, but when it is associated with other hypotensors it potentiates their action, especially in patients who have undergone sympathectomy. The mechanism by which this hypotensive effect is produced is uncertain, but the predominant, if not the exclusive, part in it seems to be played by increased sodium excretion.

Vitamin B_{12} Absorption in Pernicious Anemia: Investigations of Defect in Vitamin B_{12} Absorption Induced After Long-Continued Treatment with Some More Recent Combination Preparations. M. Schwartz, P. Lous and E. Meulengracht. Ugesk. laeger 121:353-363 (March 5) 1959 (In Danish) [Copenhagen].

The blockade in vitamin B_{12} absorption due to peroral treatment with preparations of type B_{12} plus swine pylorus mucosa has been confirmed in a large amount of material. The blockade phenomenon is frequent and often occurs after a few months' treatment. Vitamin B_{12} bound to swine pylorus mucosa is poorly resorbed, even if homologous intrinsic factor is present. Changes in the intestinal flora apparently cannot explain the blockade. It is a new phenomenon dependent on the new type of oral preparations.

Triamcinolone Myopathy. R. S. Williams. Lancet 1:698-701 (April 4) 1959 [London].

The synthetic hormone, triamcinolone, appears to be slightly more potent than prednisolone, and does not cause sodium retention. There is also evidence that triamcinolone is less likely than its precursors to induce peptic ulceration. Several side-effects have been noted, which have not been seen with other steroids. Headache, drowsiness, postprandial flushing, anorexia, and progressive loss of weight have been reported, but the most serious has been muscle weakness. The author presents 3 patients in whom muscle weakness was observed after triamcinolone therapy. Muscle biopsy was performed on 2 of them and showed widespread muscle damage. Electromyographic evidence of a primary muscle-fiber lesion was observed in all 3 patients.

In 2 of the patients weakness first appeared within 3 weeks of commencing triamcinolone therapy, and muscle power improved rapidly when prednisolone in equivalent dosage was given. In the third patient the weakness could be attributed to an exacerbation of the underlying disease, but its time of onset, the similarity of the clinical picture, and the absence of other evidence of deterioration strongly suggested that it was caused by triamcinolone. Though muscles of the shoulder girdle were affected, the weakness was greatest in those of the trunk and pelvic girdle. This proximal muscle syndrome closely resembles that seen in the muscular dystrophies and in those myopathies (presumed to be of metabolic origin) which may complicate thyrotoxicosis and carcinoma. The myopathic origin of the weakness was supported in cases 1 and 2 by the preservation of the tendon reflexes and the absence of sensory loss. In case 3 the picture was complicated by neurological signs of long standing.

In metabolic studies it was demonstrated that the nitrogen balance was similar on triamcinolone and on prednisolone therapy. The effect of the 2 steroids on calcium excretion also appeared to be much the same, and the serum electrolytes (including serum magnesium) were within normal range throughout. The author directs attention to the similarity between this myopathy and that induced in rabbits with massive doses of cortisone. He suggests that the different molecular structure of triamcinolone may potentiate this particular effect, and myopathy may thus occur with much smaller doses.

Reversible Amytrophy Complicating Treatment with Fludrocortisone. K. MacLean and P. H. Schurr. Lancet 1:701-703 (April 4) 1959 [London].

The authors present the history of a 49-year-old woman in whom severe hypotension developed after surgical removal of a craniopharyngioma. Fludrocortisone, thyroid extract, vasopressin, and other preparations were required to counteract the hypotension, diabetes mellitus, and other postoperative conditions. After treatment with fludrocortisone had been continued for about a year, the patient noticed progressive muscular paralysis, especially unsteadiness in her legs. The muscular paralysis improved dramatically on withdrawal of the fludrocortisone, and progressive recovery followed. It is suggested that, in view of the cases of muscular weakness reported with triamcinolone (9-alpha-fluoro-16-hydroxyprednisolone), the presence of a fluorine atom in the 9-alpha position in the steroid nucleus may be responsible for this complication.

Hydrochlorothiazide, A New Saluretic. J. Zatuchni, W. King and M. Resinski. Am. J. M. Sc. 237:479-487 (April) 1959 [Philadelphia].

Hydrochlorothiazide, the 3,4-dihydro derivative of chlorothiazide (the 3,4-double bond in the heterocyclic ring of chlorothiazide being saturated by 2 hydrogen atoms), was administered orally to 15 patients. In the experimental animal this compound produces a marked increase in the excretion of sodium and chloride, with relatively little increase in the excretion of potassium. The patients to whom the drug was given were all, but one, males and ranged in age from 37 to 78 years. Ten patients had coronary artery disease; 5, benign essential hypertension; one, cirrhosis and nutritional heart disease; one, phlebitis and metastatic prostatic carcinoma; one, arteriosclerosis of the aorta; and one, aortic stenosis. Eleven patients showed cardiac enlargement of variable degree. Cardiac failure, obvious or latent, was present in 6.

Dietary sodium was limited to 200 mg. daily, and a liberal fluid intake was encouraged for the patients in this series. The dose of hydrochlorothiazide was almost always 50 mg. 4 times daily; in one patient, however, it was 100 mg. and in another 25 mg. 4 times daily. The drug was given over a period of 2 to 24 days for a total of 145 patient-day observations. After treatment, 12 of the 15 patients showed a decrease in body weight, varying from one-half to 14 lb. (0.23 to 6.4 kg.) and averaging 4½ lb. (2 kg.). The remaining 3 patients showed an increase, varying from one-half to 1½ lb. (0.23 to 0.7 kg.) and averaging 0.8 lb. (0.4 kg.). The greatest loss of weight occurred among those with edema. Except for occasional weakness no symptoms were observed in patients who lost weight. Rather, there was frequently a sensation of euphoria, because breathing was much improved. Control blood pressure persistently exceeded 90 mm. Hg diastolic in 3 patients; 2 of them, who had lost 3 and 14 lb. (1.3 and 6.4 kg.) of body weight, respectively, became normotensive, and one showed no change after the treatment.

Serum concentration of sodium and chloride dropped markedly in 2 patients; in one of them a fall in serum concentration of potassium was also observed. Both these patients returned to normal when the drug was withdrawn and a regular diet was instituted. No changes were observed on electrocardiographic examination, with the exception of one patient in whom prominent U waves developed. This change, however, could have been due to underlying myocardial disease, for the serum concentrations of electrolytes were normal and there was no weight loss. The authors believe that hydrochlorothiazide, like chlorothiazide, is an antihypertensive but not a hypotensive agent and that it may produce hyponatremia, hypochloremia, hypokalemia, and hyperuricemia. The maximal dose of hydrochlorothiazide appears to be 200 mg. daily.

The Association of a Synthetic Anabolic Compound, 4-Chloro-Testosterone Acetate, with Prednisone in the Treatment of Hepatic Cirrhosis of the Morgagni-Laennec Type with Ascites. A. Bisaro, M. Casasola, C. Milesi and R. E. Genero. Minerva med. 50:449-459 (Feb. 14) 1959 (In Italian) [Turin, Italy].

The effect of 4-chloro-testosterone acetate, a synthetic derivative of testosterone, combined with prednisone, on 6 patients with hepatic cirrhosis of the Morgagni-Laennec type is described; the patients included 2 women and 4 men who ranged in age from 28 to 74 years. Ten days before the treatment, and until its end, the patients were put on a diet high in proteins and sugar and low in fats and totaling 2,470 calories per day. Prednisone was given by mouth in a dose of 30 mg. per day, divided into 3 subdoses, and 4-chloro-testosterone acetate was given intramuscularly in a dose of 50 mg. per day. With time the prednisone dosage was reduced to 10 mg. per day. Two patients, in very poor condition, died after a slight clinical improvement shown at the beginning of the treatment. The remaining 4 patients derived a noticeable benefit from the treatment; their body weight increased, their strength returned, and their general condition improved. Laboratory tests showed that diuresis had increased, ascites and edema had disappeared, the balance of minerals had become normal, bilirubinemia had decreased, cholesterol level had remained unchanged, and nitrogen had become positive. A tendency toward normal of the electrophoretic curve was observed.

Comparative Experimental Investigations on New Sulfonamides with Diuretic and "Salt-Diuretic" Effect. J. J. Chart, A. A. Renzi, W. Barrett and H. Sheppard. Schweiz. med. Wchnschr. 89:325-331 (March 21) 1959 (In German) [Basel, Switzerland].

The authors survey the different groups of diuretics available today, such as digitalis glycosides, diuretics acting by osmosis, substances that induce acidosis, xanthine diuretics such as caffeine, theobromine, and theophylline, mercurial diuretics, inhibitors of carbonic anhydrase, and others. The discovery of chlorothiazide represented a great advance in the field of diuretics. Its natruretic effect is as great as that of orally administered mercurial diuretics, and, in addition, it increases the elimination of chloride, potassium, and bicarbonate. The discovery of the diuretic effect of chlorothiazide and the well-known antibacterial and antidiabetic effects of related substances demonstrated the wide functional spectrum of the sulfonamides. In the course of chemical and pharmaceutical studies in their laboratory, the authors discovered new diuretics of high potency.

In studies on about 125 heterocyclic sulfonamides, hydrochlorothiazide was found to be the most potent diuretic. Tests on rats and dogs showed that under certain experimental conditions hydrochlorothiazide was not only up to 21 times as potent as chlorothiazide but its action was also of longer duration. In rats hydrochlorothiazide inhibited the effect of vasopressin, reserpine, syrosingopine (Singoserp), and adrenalectomy on renal function. It also inhibited the sodium-retaining effect of desoxycorticosterone acetate and aldosterone and enhanced the natruretic action of prednisolone. Its diuretic effect could be demonstrated even in dogs with experimental ascites, which is usually refractory to drugs. In addition, hydrochlorothiazide displayed antihypertensive properties in a certain form of experimental hypertension known as "adrenal regeneration hypertension." On the other hand, it had no influence on high blood pressure induced by hydrocortisone. Hydrochlorothiazide had no demonstrable effect on the gastrointestinal tract. The degree of carbonic anhydrase inhibition produced by hydrochlorothiazide in vitro was only about one-ninth that produced by chlorothiazide and, therefore, is not likely to be of any significance in the diuretic action in vivo.

These results in animal experiments were corroborated by clinical results. Not only was the natruretic effect of hydrochlorothiazide found to be 21 times as great as that of chlorothiazide, but it was also found to have hypotensive effects in human subjects. The authors conclude that hydrochlorothiazide is a new diuretic and "salt-diuretic" which is highly effective by mouth and has a low toxicity. It differs qualitatively and quantitatively from all other diuretics known so far, and these differences can be regarded as advantages in its clinical use in the various indications for diuretic drugs.

PATHOLOGY

Hyperthyroid Crisis: Clinical and Pathological Study of Two Cases. J. M. Cervino, A. Navarro, J. Maggiolo and others. An. Fac. med. Montevideo 43:166-176 (Sept.-Dec.) 1958 (In Spanish) [Montevideo, Uruguay].

Two women, 33 and 40 years old, respectively, with diffuse exophthalmic goiter were hospitalized in the Hospital of the University of Montevideo. In both cases the goiter was large and with intense thrill. In the younger patient acute symptoms of hyperthyroidism appeared 3 months before the consultation. The treatment then consisted of Lugol's solution, in daily dosage of 10 drops, which since it did not modify the symptoms was discontinued on hospitalization. An unexpected hyperthyroid crisis developed on the 7th day after admission. It progressed rapidly, with mental confusion, violent tachycardia, fever, vomiting, and dyspnea complicated by a genital hemorrhage and bilateral pneumonia. The symptoms did not respond to treatment, consisting of sedatives, iodine, cortisone, and the parenteral administration of liquids, and the patient died 6 days after commencement of the crisis. In the older patient hyperthyroidism had lasted for a year and a half. Early in the course of the disease the patient was treated with radioiodine (I^{131}) in a total dosage of 10,000 μc. As a result of this treatment the symptoms were nearly under control, but the size of the goiter was not modified. On admission, the patient was given Lugol's solution, in daily dosage of 15 drops, as preoperative treatment for a thyroidectomy. *During the first 20 days of this treatment* she lost 10 kg. (22 lb.) in weight. A hyperthyroid crisis developed on the 20th day, with vomiting, diarrhea, fever, anxiety, and general diffuse pruritus. The symptoms did not respond to treatment with cortisone and other medicaments used in the first case, and the patient died 12 days after the crisis started.

In both patients the hyperthyroid crisis appeared suddenly and without any apparent cause. Fever was high, but the patients did not perspire. Findings on autopsy consisted of thymolymphatic hyperplasia in one patient and subinvolution of the thymus in the other. Degeneration of the liver and atrophy of the suprarenal cortex were found in both patients. The authors believe that there is a *relationship between the hyperthyroid crisis* exhibited by the patients and the thymic, hepatic, and suprarenal lesions found at autopsy. Discontinuation of iodine treatment in the course of thyrotoxicosis in one patient and administration of the drug to the other after subsidence of the symptoms may have acted as causal factors in rapid aggravation of the visceral lesions which resulted in development of the hyperthyroid crisis.

Chordoma. E. Mauritzen, P. M. Christiansen and F. Zachariae. Nord. med. 61:368-371 (Feb. 26) 1959 (In Danish) [Stockholm].

Chordoma is a rare, histologically well-characterized tumor which occurs along the axial skeleton, most often at the base of the cranium and in the sacral region, growing slowly, expansively, and invasively. Cranial chordomas usually appear at the age of 30 to 40, and sacral chordomas at the age of 50 to 60, but the tumors may occur at any age and are twice as frequent in men as in women. The cause is unknown; etiological significance has been ascribed to trauma. The tendency to metastasis is slight. Subjectively and objectively, the cranial forms give the same symptoms as other intracranial tumors with the same localization. In the vertebral tumors the first and most frequent symptom is backache; later there are motor and sensory disturbances due to pressure on the nerve roots and medulla. The initial symptom in the sacral tumors is most often vague and intermittent pain in the anal region; in the final stages the pain may be more violent and almost intractable. The chordoma shows all transitions, from torpid to fulminant course, and the degree of malignancy can apparently not be judged on the basis of the histological picture. By its growth the tumor causes bone destruction, seen roentgenologically as clarifications with sharp contours. In the cranium ventriculography and in the spinal column myelography can often reveal the tumor. The sacral tumors can sometimes be recognized only on rectal exploration when they are small and presacral.

Preoperative diagnosis of chordoma depends on histological examination. Biopsy, best by aspiration, can be undertaken only with tumors in the sacral region or in the nasopharynx. Macroscopically the tumor is rounded or lobulated, voluminous, firm, and grayish white. On cross section, it is seen to be gelatinous, semitransparent, sometimes containing cysts with mucoid substance. Hemorrhages and necrosis in the tumor are common. The microscopic picture is typical. Treatment is surgical. Radical excision is practically never feasible in cases with sphenoccipital localization. In the sacral cases laminectomy should be performed with resection as high as possible; sacral nerves II and at all events one sacral nerve I must be left. The intervention must be attempted even with small tumors. Recurrence in the course of months and death in the course of years are the rule. On recurrence, excision must be repeated; cases with repeated excisions through a period of years are not uncommon. Where extirpation is impossible, roentgen-ray treatment may lessen, sometimes stop, the pain for a time. Usually patients do not seek medical aid until 2 or 3 years after the first symptoms appear. Two cases of cranial and 3 of sacral chordoma are described.

Involvement of the Liver in the Course of Diseases of the Kidney. A. Vercellone, P. F. Angelino, I. Oddone and F. Linari. Minerva med. 50:475-482 (Feb. 17) 1959 (In Italian) [Turin, Italy].

The pathological involvement of the liver during the progressive stage of certain diseases of the kidney was studied in 58 patients who were free from a primary disorder of the liver. Acute or subacute glomerulonephritis was present in 11 patients, chronic glomerulonephritis in 25, polycystic kidney in 3, kidney disease of urologic origin in 11, and acute anuric tubular disease in 8. Enlarged liver was found in 38 instances (66%); the single hepatic flocculation test was positive for involvement of the liver in 22 patients (55%), and the multiple hepatic flocculation test was positive in 18 (31%). Alteration of the protein composition, being limited to albumin and globulins only, was observed in 28 of the 50 examined patients (56%); alteration of the prothrombin time was observed in 8 of the 23 examined patients (28%). Bilirubinemia values were found to be normal in all instances.

The incidence of enlarged liver was high and uniformly distributed among all patients regardless of the severity of the kidney's lesion. Hepatic flocculation tests revealed involvement of the liver at a higher degree among patients with acute glomerulonephritis than among those with other kidney diseases; these tests also had a prognostic value in the sense of reflecting the progressive course of the disease rather than the extent of the produced damage. Alteration in the flocculation tests was observed in less degree among patients with chronic glomerulonephritis. Protein composition was altered to almost the same extent, as the result of flocculation tests, in patients with acute glomerulonephritis, and to a greater extent in those with chronic glomerulonephritis. The anatomico-pathological [illegible] and functional findings was limited to the few instances in which autopsy was performed; there seemed to be revealed a higher incidence of liver involvement than the clinical and functional examinations indicated. This investigation has thus suggested the pathological involvement of the liver in patients with certain diseases of the kidney.

PHYSIOLOGY

The Use of Methionine, Pyridoxine and Unsaturated Fatty Acids in Coronary Atherosclerosis. P. E. Lukomsky. Sovet. med. 23:14-21 (no. 3) 1959 (In Russian) [Moscow].

The author studied the action of methionine, pyridoxine, and unsaturated fatty acids on the indexes of lipid and protein exchange in patients with coronary atherosclerosis. Methionine was employed in a daily dose of 6 Gm. for 20 days. The dosage of pyridoxine was 50 to 100 mg. daily for 10 to 20 days. Unsaturated fatty acids were used in a mixture with ethyl ethers of linoleic and linolenic acids (20 ml. a day for 20 days). Administration of the above agents produced in the majority of patients a reduction in the blood cholesterol level, a rise in the lecithin content, an increase in the lecithin cholesterol correlation, and a drop in the beta-lipoprotein fraction. The total quantity of blood proteins did not undergo any noticeable change. The albumin content increased slightly, while the globulin fractions decreased.

BOOK REVIEWS

The Physician and Group Practice. Edited by Edwin P. Jordan, M.D. Cloth. $6.75. Pp. 238. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

Since World War II group practice has become a subject of widespread interest and discussion. Despite this, there have been few really useful publications on the subject. This book fills the void. It is biased in favor of groups, but that is what is intended and this enhances its value. In spite of this bias, arguments for and against groups are ably brought out. Starting with a brief, but pertinent, historical chapter, the reader is led through a series of interesting and useful discussions of practically all of the topics concerning group practice. The various forms of group structure are discussed and evaluated in a meaningful way. How to start a group and whether to join one are questions that are explored in a helpful manner. Problems encountered in groups, benefits gained from them, steps to take in solving problems, and methods of working through difficulties encountered are all explored and discussed from experience.

The chapters directed to the physician contemplating joining a group are especially good. Guides for evaluating one's own personality and how it might fit into a group practice are presented. Certain points are made about how a group works, about interrelationships of members in a group, and personal satisfaction which can be gained through group practice that could help crystallize one's thoughts in favor of group practice. The constant source of stimulation and education that can be derived through association with colleagues in an informal and formal manner in a group clinic may appeal to many physicians. On the other hand, certain drawbacks should be carefully considered. The chance to advance one's income in an outstanding way is seldom found in a group clinic since income distribution is rarely contingent on bookings alone. Also the opportunity to forge ahead and fulfill a strong desire for personal recognition is not as readily available as in private practice. A group situation is not the best one for a "rugged individual," a man who thrives on competition, or one who wishes to be self-employed. Of necessity, a certain amount of cooperation and harmony must be achieved to promote a successful clinic. These are all factors to be considered and evaluated when contemplating association with a group, and many more are found in this book.

For the group already established there are several chapters which should prove useful. Discussions on internal problems encountered and various solutions to these problems are described. Income distribution is discussed, and suggestions as to effective ways of solving this problem are pointed out. The business side of the clinic is dealt with in detail. These discussions are all by men who are well qualified in their respective fields. Nonessentials have been eliminated and the discussions are brief and to the point. The book is well written and the style is conducive to easy reading. From the first chapter, in which a brief history is found, to the last chapter, which covers the relationship of the clinic and the individual staff member to the community, the reader finds a comprehensive discussion and helpful suggestions.

Treatment of Cancer and Allied Diseases. Volume III: Tumors of the Head and Neck. By seventy authors. Edited by George T. Pack, M.D., F.A.C.S., and Irving M. Ariel, M.D., F.A.C.S. Second edition. Cloth. $30. Pp. 781, with 1028 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1959.

The authors of this volume, which is part of a series of nine volumes now going into its second edition, hail chiefly from the United States and Canada, but include a number from other centers throughout the world. Most of the names are widely known and respected by those interested in this field.

This volume consists of seven sections divided into 52 chapters. It would be difficult to praise it too highly. Elegantly prepared, lavishly and beautifully illustrated, it is what it claims to be, an authoritative statement of today's treatment of tumors of the head and neck. It should be useful for a long time to come.

Burns: Pathology and Therapeutic Applications. By Simon Sevitt, M.D., M.Sc., M.A. Cloth. $7.50, 37s. 6d. Pp. 364, with 85 illustrations. Butterworth & Co. (Publishers) Ltd., 88 Kingsway, London, W. C. 2, England; 1367 Danforth Ave., Toronto 6, Canada, 1957.

In this volume the author deals primarily with the clinical pathology of burns and, where possible, correlates in a most comprehensive manner the interrelationship of physiological derangements, the clinical findings, and therapy. Major emphasis is placed on organs and systems consistently involved in pathological processes secondary to burns. The bibliography is chosen with care to include only reports that have a definite impact on the subject. The illustrations and charts are excellent and ade-

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

quately explained. The mortality of severe burns has not improved in the past 10 years. Attempts to favorably alter statistics have been confined in the most part to improvement or, at least, change in therapy. For the first time an author has approached the impasse by reviewing known pathological changes and their possible cause. This book is an outstanding contribution to medical literature and should be of tremendous value to all physicians interested in the proper management of burns.

A Manual of Anæsthetic Techniques. By William J. Pryor, M.D., Ch.B., F.F.A. With foreword by the late J. H. T. Challis, M.R.C.S., L.R.C.P., F.F.A. Second edition. Cloth. $7. Pp. 228, with 75 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; John Wright & Sons, Ltd., 42-44 Triangle West, Bristol 8, England, 1959.

A number of changes in this primer have resulted in a more modern textbook, although the first edition was written only four years ago. The chapters and content remain essentially the same, except for the inclusion of new agents.

This book is intended primarily for British schools of anesthesia, and for "house" surgeons and "registrars" commencing the practice of anesthesia. Yet it is written so concisely that it lends itself to easy reading by students of medicine, interns, residents, and nurses. The organization of the book is excellent, touching on all the basic problems of anesthesia. There are good photographs and line drawings which are correctly used. The printing and general layout are excellent. The content is somewhat superficial and, while this is, of course, good for the novice, it is of disadvantage to those further along in their training. The book could be improved by amplifying the bibliographies. It can be recommended to nurses, interns, and residents who wish to read a simple and concise presentation of British views on anesthesia.

Pulmonary Circulation: An International Symposium, 1958, Sponsored by the Chicago Heart Association. Edited by Wright R. Adams, M.D., and Ilza Veith, Ph.D. [Impetus and financial assistance for symposium provided by Chicago Heart Association. National Heart Institute, National Institutes of Health, U. S. Public Health Service, contributed to cost of publication by means of grant no. H-3927.] Cloth. $4.50. Pp. 316, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1959.

This is a record of the proceedings of an international group of physiologists, pathologists, and clinicians gathered to consider the pulmonary circulation in health and disease. It consists of a series of carefully written papers, illustrated with photographs and diagrams and accompanied by a transcript of the ensuing viva-voce discussion. An interesting introductory chapter sketches the history of the pulmonary circulation, especially the remarkably explicit statements on the subject by Michael Servetus in the years before his tragic death in 1553. Six chapters deal with the physiology of the pulmonary circulation and emphasize the complexity of the factors that determine the pressures, rates of flow, and distribution of blood in the lungs. Six chapters on pathology deal especially with the relation of the pulmonary to the bronchial vascular systems and the significance of pulmonary and systemic hypertension. Five chapters on pulmonary circulation in primary disease of the lungs include discussions of the circulatory disturbances in tuberculosis and emphysema. The two last sections consist of seven and six chapters on the pulmonary circulation in congenital and in acquired heart disease respectively.

This book contains much of fundamental importance, if not of immediate practical value, to the physician. Reading is made unnecessarily difficult by occasional oversights. For example, the conscientious student will be puzzled by the confusion of Aryanism with Arianism on page 3 and by the redundant symbols in the mathematics on pages 26 and 63. The reader who picks up the book after an interruption may be baffled by abbreviations like C. C. P. and T. M. P. If he traces them back to where they are first used he may or may not find them expanded. This loss of time could be prevented by appropriate entries in the index, which is otherwise excellent. The book as whole is attractive and inspiring.

Peripheral Vascular Diseases: An Objective Approach. By Travis Winsor, M.D., F.A.C.P., Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles. With foreword by Burrell O. Raulston, M.D. Cloth. $16.50. Pp. 845, with 435 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1959.

It is obvious on reading this book that the author is a well-seasoned, experienced medical teacher. Great pains have been taken to make a difficult subject interesting and easy to understand. There are over 400 illustrations to supplement a well-written, concise textbook. The presentation of material is well planned. After sections on the anatomy and physiology of the circulation of the arms and legs, several chapters are devoted to the techniques that are employed as diagnostic aids. Two chapters show exactly what points are to be covered in taking a patient's case history and in making a physical examination. After a classification of peripheral vascular diseases, each disease is taken up in detail, following the same order of age, sex, race, etiology, history, physical examination, laboratory studies, diagnosis, differential diagnosis, and treatment. Selected references are listed at the end of each chapter.

This is one of the most clearly written as well as comprehensive textbooks on peripheral vascular diseases published in many years. It can be read with pleasure as well as profit by any physician who treats patients with peripheral vascular disease and should be particularly valuable to students and medical residents.

"Allergic" Encephalomyelitis. Proceedings of a Symposium: Experimental "Allergic" Encephalomyelitis and Its Relation to Other Diseases of Man and Animals. Edited by Marian W. Kies, Ph.D., Chief, Section on Biochemistry, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland, and Ellsworth C. Alvord, Jr., M.D., Associate Professor of Neurology and Pathology, Baylor University College of Medicine, Houston. Cloth. $13.50. Pp. 576, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The concept that allergic inflammation of organs may be the result of intrinsic causes in addition to those of extrinsic origin (pollen, molds, dust, foods, drugs, etc.) has attracted serious investigators, particularly in recent years. This concept presumes that the organism can produce antibodies to one of its own organs or tissues, probably as a result of some previous damage to that organ, such as by infection, drugs, or trauma. It is presumed further that such an antibody then reacts with the specific antigen in the healthy organ, producing an allergic inflammation. Such a mechanism has been demonstrated clinically, notably in certain hematological conditions and eye inflammations, and experimentally in a number of organs, such as testes, adrenals, thyroid, and kidneys, formed blood elements, and the nervous system.

Such a concept, which might possibly explain various types of encephalomyelitis and other demyelinating diseases, has received attention experimentally from a large group of investigators. The symposium recorded in this volume represents an exchange of their ideas and experience by 60 significant contributors to this field. The usual method of producing "allergic" encephalomyelitis is by the injection of brain homogenates with Freund's adjuvant. The symposium takes up the subject from three major aspects: (1) clinical and pathological correlations of human and experimental encephalomyelitis, (2) attempts to identify the substance in nervous tissue responsible for the antigenic effect, and (3) immunological aspects, dealing with circulating antibodies, passive transfer, delayed hypersensitivity, and immune tolerance phenomena.

This volume constitutes the essence of experience and thinking on an important segment of autosensitization. It is an up-to-date reference book on a subject which should be of particular interest to immunologists, pathologists, neurologists, specialists in infectious diseases, allergists, and all physicians who are visionary enough to realize that auto-sensitization may prove to be one of the most important factors in the etiology of human disease.

Fundamentals of Otolaryngology: A Textbook of Ear, Nose and Throat Diseases. By Lawrence R. Boies, M.D., Professor of Otolaryngology, Chairman, Department of Otolaryngology, University of Minnesota Medical School, Minneapolis. Associates: Anderson C. Hilding, M.D., and others. Third edition. Cloth. $8. Pp. 510, with 212 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

The authors of this textbook call it a guide for medical students and nonspecialist practitioners. It is safe to say that those more advanced, namely at the residency level and even in the early years of practice, will find much in it that is useful. To the clarity and conciseness of the text is added a profusion of illustrations, for the most part original, and all interesting and well selected. Preceding the discussions on things clinical are sections on applied anatomy and physiology, which are very well done and could grace a larger reference textbook.

It is not easy in an era of rapid change like ours to eliminate outmoded pictures of pathological states and obsolete therapeutic measures. The authors have, however, fully recognized the impact of antibiotics and other agents on altering the appearance, course, and treatment of suppurative conditions, among others, which once were such an important part of disease in otolaryngology. The surgical attacks on deafness, and our present-day handling of carcinoma in this region are likewise adequately discussed. Each chapter ends with an up-to-date list of references to the literature.

Medical Department, United States Army. Surgery in World War II: Hand Surgery. Edited by Sterling Bunnell, M.D. [Prepared under direction of Major General George E. Armstrong, Surgeon General, United States Army.] Colonel John Boyd Coates, Jr., editor in chief. Prepared by Historical Unit, Army Medical Service, under direction of Colonel Calvin H. Goddard. Associate editor for hand surgery: Mary E. McDonald; assistant editor: Janie W. Williams. Office of Surgeon General, Department of Army, Washington 25, D. C. Cloth. $3.75. Pp. 447, with 224 illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1955.

The importance of hand wounds was not properly recognized until after World War I. As a result of the increased interest in such cases between the two world wars, a number of special centers for the treatment of these injuries were established in World War II both in the United States and overseas. Many of the techniques devised, especially for tendon repair and restoration of lost members or functions, were highly successful. In addition to treatment, many ingenious prosthetic appliances were developed for these patients. The editor of this volume was civilian consultant for hand surgery to the Secretary of War. Such outstanding surgeons as C. W. Cutler Jr., Sterling Bunnell, H. S. Allen, and Mather Cleveland contributed chapters. The book is well written and printed on paper of a high quality. It is illustrated with photographs and line drawings. There is an index.

QUESTIONS AND ANSWERS

PAINFUL HAND

To the Editor:—*A 50-year-old woman complains of severe, boring pain over the dorsum of the right hand and extending to the dorsum of the fingers. This has been present for several years. Initially there was also elbow involvement. There were periodic recurrences, with improvement after several days, and it was years before she consulted a physician. A year and a half ago, the pain in the hand became quite marked, and there has been little improvement since. The pain comes only at night, starting 15 minutes after the patient goes to bed. Relief comes in one or two hours if she sits up in a chair. Normal motor and reflex functions of the right fingers, forearm, and arm are present. The patient is in good health otherwise. Complete examination by a neurologist on three separate occasions has revealed normal findings except for questionable, mild, altered appreciation of light touch and pin prick over the dorsum of the hand. No trophic changes have been noted. Cervical spine x-rays have been normal on several occasions, as have findings on chest x-rays, routine hematological indexes, and special x-rays of the apices of the lungs.*

Homer B. Martin, M.D., Louisville, Ky.

Answer.—The symptom of pain in the arm and hand that occurs when the patient lies down and is relieved when she sits up makes one think of some type of pathological involvement of the brachial plexus, subclavian artery, and thoracic outlet. The information given seems to indicate that a diagnosis of supernumerary rib has been ruled out. One must think first of a condition in which paresthesias and pain develop in the hands and arms because of compression of the subclavian artery and vein and the brachial plexus beneath the coracoid process of the scapula and stretched pectoralis muscle, the so-called subcoracoid-pectoralis minor syndrome. A second condition to be considered is that described by Falconer and Weddell, in which the subclavian artery and the brachial plexus are compressed between the clavicle and first rib by hyperextension of the neck and posterior abduction of the shoulders. In this condition, elevation of the first rib causes narrowing of the space between the first rib and the clavicle with hyperextension of the neck and produces compression of the brachial plexus and subclavian artery. One must also rule out the possibility of an intraspinal lesion, such as spinal cord tumor. These syndromes are more prone to occur in patients of middle age because of loss of tone in the elevator muscles around the shoulder and neck. Heat, massage, and corrective posture exercises for the neck and shoulders, as well as resistance exercises to strengthen the shoulder elevator and retractor muscles, may be given with expectation of some benefit. In addition to this, general posture training should be advised.

ARTERIOSCLEROTIC DISEASE

To the Editor:—*What is the current opinion regarding use of vitamin E and/or lecithin in arteriosclerotic cardiovascular disease? It was my impression it was found ineffective, and therefore abandoned, about 1946 or 1947. Recently several patients have asked about it and say they have heard good claims for it.*

Donald W. Maclean, M.D., Hamilton, Mont.

Answer.—There is little acceptable scientific basis for using vitamin E and/or lecithin in the treatment of arterioscleriotic cardiovascular disease. There are so many possible causes of cardiovascular disease and arteriosclerosis that one cannot say they are directly related to a single vitamin or other substance in the diet or may be prevented by any specific dietary approach. The cause of cardiovascular disease is believed to be related to many factors, including age, sex, heredity, diet, activity, and possibly others.

LATE SYPHILIS AND PENICILLIN SENSITIVITY

To the Editor:—*What is the accepted best treatment for late syphilis in a patient allergic to penicillin?* *C. M. Creswell, M.D., Kenosha, Wis.*

Answer.—It is necessary to evaluate the history of hypersensitivity to penicillin carefully to ascertain its validity and to determine by detailed examination just how important it is to give maximal antisyphilitic therapy. If penicillin sensitivity is verified, such a patient should be given one of the broad-spectrum antibiotics of the tetracycline group, 2 Gm. per day for 10 days to two weeks. At the other extreme, in a patient with taboparesis, for example, with primary optic atrophy, spinal fluid showing elevated cell count and protein level, and unverified history of sensitivity to penicillin, a proper course of action would probably be to start the

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patient on steroid therapy and shortly thereafter begin penicillin therapy in adequate dosage, continue to give steroids with a gradual tapering in dosage for a week or two after the penicillin therapy has been completed, and then to watch carefully for possible appearance of allergic reaction; steroid therapy may be reinstituted if necessary.

SEIZURES IN INFANT TWINS

To the Editor:—*Identical twin boys had seizures several hours after their second diphtheria, tetanus, and pertussis immunizations at the age of 6 months. The seizures occurred simultaneously, between the solid and liquid portions of a meal, and were preceded by several minutes of irritability and crying, with no particular provocation. Then rolling back of the eyes and extension and stiffening of the neck and back occurred, followed by clonic movements of the arms, legs, and head. Some pallor, but no cyanosis, was present. The babies were unresponsive during the seizures, which lasted about two minutes and were followed by lethargic consciousness during which they finished their bottles and then slept for two hours. Phenobarbital elixir, 1 teaspoonful twice daily, was given for several days after this and subsequent seizures. The second seizure was also simultaneous in both and occurred two weeks later. Fever has never been present. One twin has had three more essentially similar seizures at the ages of 10 months, 13 months, and 13½ months. The other twin has had no further seizures, but no attempt has been made to detect nocturnal occurrence. Electroencephalograms, done on both at the age of 10½ months, were normal. The twins were born in uneventful multiparous delivery and seem normal in physical and mental development. There is no familial history of epilepsy. Does this seem to be idiopathic epilepsy in spite of the normal electroencephalographic tracings? May these tracings and the apparent failure of one twin to have further seizures be interpreted as favorable prognostic signs, even if idiopathic epilepsy is present? Should the twin who has had additional seizures be continued indefinitely on phenobarbital therapy? Is it advisable at this time to subject one or both to lumbar puncture and blood and x-ray diagnostic studies? There has been no neurological consultation.* *M.D., Illinois.*

Answer.—The occurrence of seizures at the age of 6 months is suggestive of symptomatic rather than idiopathic epilepsy. There is nothing in the description of the individual seizures that would suggest a focal onset. The normal electroencephalograms are not helpful, since this merely means that at the time of sampling no abnormal patterns were present. Since tracings were taken on only one occasion and were normal at that time, further tracings should be obtained. That one twin had two seizures two weeks apart and has had none for the past three and one-half months without medication is a favorable prognostic sign. The other twin, who has had subsequent seizures to a total of five, should certainly have medication continued for at least a year. In view of the complexities of this particular situation, it is definitely advisable to have these children studied carefully by a neurologist and to have a complete laboratory examination. Intracranial as well as metabolic diseases must be considered in these children.

ABSORPTION OF ALKALI

To the Editor:—*Can one use too much alkaline water by drinking and bathing in it? A mineral springs resort caters to people who have such diseases as rheumatism, arthritis, and bursitis, and many seem to show good results. The resort provides hot mineral water, mud baths, and special diets. A number of patients have asked if the body can absorb too much alkaline product.* *Alice S. Cutler, M.D., Los Angeles.*

Answer.—This consultant is unaware of any scientific evidence that use of alkaline water is of benefit to people who have rheumatism, arthritis, and bursitis. It is extremely doubtful that the body could absorb too much so-called alkaline water. A normal, healthy body is well equipped to utilize efficiently the food and water ingested regardless of alkaline or mineral properties. It is probably a good thing that the body has the ability to resist most efforts of the uninformed to tamper with the pH of its fluids. It is not felt that the patients referred to need be concerned over the use of alkaline water in drinking and cooking. No toxic effects are known. There is no evidence that minerals in such waters are absorbed through the intact skin.

CONGENITAL DEFECTS

To the Editor:—*A premature baby weighing 4 lb. (1,814 Gm.) had the following defects: exstrophy of the urinary bladder, prolapse of the ileum, agenesis of the colon, atresia of the anus, lack of fusion of Müller's ducts, absence of external genitalia, lumbar spine bifida, meningocele, club feet, and absence of the lower abdominal wall. In view of the fact that most of these defects occurred in the same region, please specify at what embryonic age and what area was affected.*

M.D., Connecticut.

Answer.—The inhibitions of development described can be ascribed to abnormal conditions in utero toward the end of the fourth week after conception, when the pelvic region is growing especially rapidly. A severe illness of the mother four to six weeks after the last menstrual period might be responsible. Another possible cause is a severe dietary defect. In rats, similar abnormalities have been produced by completely removing folic acid from the mother's diet for a brief period early in pregnancy (Nelson and others, *J. Nutrition* 56:349, 1955).

SALT AND BALDNESS

To the Editor:—*Is there any relationship between the amount of salt ingested in the diet and the development of baldness? There have been newspaper reports of a Scandinavian physician who makes such claims. Also, can the injection of vitamin B_1 prevent mosquito bite?*

Juan Silverio, M.D., Marianao, Cuba.

Answer.—No scientific evidence has been seen that indicates ingestion of salt has any effect on balding. Apparently this is a finding of one Scandinavian physician. No cogent scientific evidence has appeared indicating that thiamine has any mosquito-repelling effect.

DISSEMINATED CHOROIDITIS

To the Editor:—*A patient has choroiditis of unknown cause with numerous scotomas, each corresponding to a white patch in the choroid. His central vision is 20/30 in each eye. The scars on the choroid are not outlined by any pigment. There are no cells in the vitreous and no pigment deposits around the periphery of the patches. It is not known whether any arterioles are constricted, but there have been hemorrhages in the past that have cleared up. There are no opacities except when there are hemorrhages. The peripheral vision is good except for small, fast-moving objects, such as a golf ball in flight. Vision is good except at night and in bright sunlight. It is much better on an overcast or cloudy day. There are no opacities in the lens. His greatest difficulty is photophobia, especially when the sun is low in the sky. His adaptation to dark is poor. He suffered severe sunburns in early youth, and it is questioned whether this could be a factor. This condition has been present at least 15 years. Is there any way to overcome the photophobia, which interferes with driving a car? Is driving permissible under these circumstances? Is there anything besides dark glasses that can be used? Is there any drug that would be of help?*

M.D., New York.

Answer.—The patient apparently has disseminated choroiditis. The retention of good central vision speaks against a congenital disease such as choroideremia or gyrate atrophy. The recurrent hemorrhages also are evidence of an active, acquired process. The "white patch" is probably sclera shining through areas of choroidal atrophy. Since these are old, healed areas, it is unlikely that any form of therapy will change them. Symptomatic aid is also difficult. Night vision is already poor, and, theoretically, dark glasses should not be worn, since all tints reduce the transmission of light. However, one a practical basis, it has been observed that the yellow, so-called shooter's glasses are of aid at dusk in that the contrast of objects against a neutral background is improved. These might be tried here. There may also be an optimal pupil size for this patient, and weak solutions of miotics or mydriatics may be tried.

It is unlikely that severe sunburn in youth is related to the present problem. Intense sunlight may produce a keratoconjunctivitis or a macular lesion (eclipse scotoma) but not a choroiditis. Finally, as long as central vision is 20/30 and the peripheral extent of the visual field is normal, it would seem unfair to proscribe driving an automobile.

VITAMINS IN CANNED FOODS

To the Editor:—*How much loss of vitamins B and C is there in canned and in frozen fruits, vegetables, and fruit juices?*

F. L. Troost, M.D., Holt, Mich.

Answer.—According to the available information, there is little loss of vitamin B complex and vitamin C in the canning of fruits, vegetables, and fruit juices. From the nutritional standpoint, canned or frozen and fresh vegetables are usually considered interchangeable.

LONG-TERM ANTICOAGULANT THERAPY

To the Editor:—*A 54-year-old man is now in the fourth week of his second myocardial infarction. The first occurred eight and one-half years ago. At that time he received no anticoagulants. He made an uneventful recovery and worked as usual until the second infarction. He is making an uneventful recovery and is receiving anticoagulants. He is highly emotional, and now and for some time to come he will be under considerable emotional strain. Should he be given a permanent course of anticoagulant therapy?*

M.D., New Jersey.

Answer.—The subject of long-term anticoagulant therapy is still controversial. It is this consultant's present practice to maintain long-term anticoagulant therapy, where possible, in all patients who have sustained more than one myocardial infarction. This is based on published reports and personal impressions suggesting that the recurrence rate and mortality are reduced by this therapy. This is difficult to prove statistically, but follow-up studies appear to show an improved prognosis in treated as compared to untreated patients. In the case cited, it is recommended that permanent anticoagulant therapy be continued, particularly because of the stresses to which the patient will be exposed. It is assumed that he will cooperate fully in regulation of the anticoagulant dosage by having regular prothrombin time determinations.

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MOTH CRYSTAL DERMATITIS

To the Editor:—*Please give information relating to moth crystals (paradichlorobenzene) as a cause of severe dermatitis.* *M.D., Massachusetts.*

Answer.—Paradichlorobenzene occurs in colorless crystals which are used for moth-proofing and other purposes. In undiluted form, it is a strong irritant for human skin. Cases of severe allergic dermatitis due to this substance have been described. The concentration for patch testing to ascertain whether allergic hypersensitivity exists is a 1% solution in alcohol. In addition to the cutaneous reactions produced by paradichlorobenzene, allergic asthma and, after continued exposure to its vapors for years, hepatitis and cataract have been described.

CANCER METASTASES

To the Editor:—*A patient had adenocarcinoma of the kidney a year ago. The kidney was removed, and x-ray treatments were given. Now she has multiple metastases in the abdomen, and she has had another series of x-ray treatments. Are there any favorable reports on use of radioactive gold in similar cases? What other treatment might be given?*

Roy F. Messinger, M.D., Circle, Mont.

Answer.—This consultant knows of no treatment which will offer much in this situation. Nitrogen mustard and thio-tepa, given intraperitoneally if the metastases are small, or intravenously if they are large, might have some palliative value.

ALOPECIA DUE TO PONY TAIL

To the Editor:—*Could wearing the hair in pony-tail style cause alopecia?*

C. W. Jacobson, M.D., Breckenridge, Minn.

Answer.—The pony tail and other forms of hair style resulting in constant traction on the pilary apparatus are capable of producing alopecia. In former years, various marginal types of hair loss were occasionally observed as a result of tight braiding and the use of bobby pins, hair curlers, and similar devices that produced a constant pull on the hair shaft. Recently, a number of instances of marginal hair loss, as well as diffuse central alopecia, have been observed as a result of the constant pull on the hair shaft resulting from the pony tail and similar hair styles.

FAT CONTENT OF SEMEN

To the Editor:—*In answer to the question on coloring of seminal fluid, which appeared in* The Journal, *Dec. 20, 1958, page 2207, the consultant stated that normal semen contains "lecithin, cholesterol, and phosphorized fat." During a discussion with a young married woman on the many facets of "married life," she stated that she enjoys fellatio. It occurred to me that she may be ingesting as much highly concentrated fat each time as would be contained on an untrimmed large steak. This may account for her having trouble losing weight, even though she declares she is watching her diet rigidly. She also has noticed increased development of her breasts. Is there a possible hormonal factor of testosterone or another undiscovered hormone which may be aiding in this reaction and might be helpful to others? Obviously, the imagined or real need for help in this area is costing American women and their husbands millions of dollars each year as well as much emotional turmoil. In Beardwood's chapter on obesity (in Cyclopedia of Medicine, Surgery, Specialties, edited by G. M. Piersol, Philadelphia, F. A. Davis Company, 1958, vol. 9, pp. 813-825), the possibility of the body converting some portion of protein into carbohydrates is stressed. Is there any newer thought along this line? Some people seem to get fat on air alone, or is this the bloating of starvation?*

G. H. Horner, M.D., York, Pa.

Answer.—As far as this consultant is aware, while there may be some psychogenic and genetic factors concerned with obesity, it generally can be ascribed to intake of more calories per day than are expended. No cogent scientific evidence is known indicating that body fat is accumulated in any other way; in order to remove fat it is necessary to ingest fewer calories than one expends. It should be remembered that calories are obtained from protein and carbohydrate as well as from fats. In regard to the possibility of fellatio being a contributing factor in obesity, one would be somewhat skeptical. Even assuming an ejaculation of 10 cc. of semen were all fat, this would be only 90 calories. It is extremely doubtful that this would have a significant effect on inability to take off weight unless, of course, it was practiced several times a day. A useful pamphlet on weight reduction can be obtained for distribution to patients by writing to the Council on Foods and Nutrition, American Medical Association.

WASHINGTON NEWS

International Health Developments . .
Officials Criticize Age Discrimination . .
Officials of Aging Conference . .
Testimony on Insurance Bill . .
HEW Release Policies . .

INTERNATIONAL HEALTH LEGISLATION

Congress was asked to make sure that the proposed international medical research program deals strictly with research efforts and not with medical services.

A pharmaceutical industry official told a House commerce subcommittee that "the implementation of a research effort must be . . . kept administratively and otherwise entirely separate from anything in the nature of a point four [economic assistance] program, however worthy." The witness was Francis Boyer, chairman of the board of Smith Kline & French Laboratories.

The subcommittee, headed by Rep. Kenneth Roberts (D., Ala.), is considering a Senate-passed bill that would set up a new National Institutes of Health for international medical research activities that would be financed by a 50-million-dollar annual authorization.

Boyer also recommended that foreign nations put up matching funds "to lessen any tendency . . . on the one hand to feel that they might as well get on board Uncle Sam's gravy train, or at the other extreme actually to resent what they might call American control of their research with a real and fancied dislocation of their academic salary structure."

Precautions should be taken that United States funds are not used to subsidize the product development of foreign commercial houses, and "grants or contracts under the bill should be confined to academic and other nonprofit centers and individuals," said Mr. Boyer.

The program should proceed slowly and on a small scale at first, he said, partly because of the desirability of balancing the budget and partly because of "some apprehensions as to our supply of medical manpower."

The American Medical Association supports the legislation and has also said the emphasis should be on research, not services, as the measure states.

In another development President Eisenhower expressed some misgivings about another international program with medical implications—the so-called great white fleet plan to send reserve Navy hospital and other ships abroad to aid nations hit by epidemics and other disasters. The chief executive said he is "always suspicious of helpful plans" that originate solely with the donating nation. Under the foreign aid program, he noted, countries needing and desiring help draw up their own plans and suggestions as to how the United States might assist them.

Meanwhile, the foreign aid authorization bill signed by the President contained a provision authorizing at the chief executive's discretion the spending of 2 million dollars for research into possibilities of eradication of diseases.

And a Senate government operations subcommittee issued a report, "Cancer: A Worldwide Menace," that stated, in part, "The evidence is clear that cancer is a world problem, best solved by research on a world basis."

AGE DISCRIMINATION IN EMPLOYMENT CRITICIZED

Federal officials told Congress that mandatory retirement ages and age discrimination in employment are two major problems that need to be solved to help elderly persons lead more useful lives.

Testifying before the special Senate subcommittee studying problems of the aged, witnesses from the Labor Department and the Civil Service Commission said that arbitrary industry standards on employees' ages add to the problems of the elderly.

O. Glenn Stahl, director of the Civil Service Commission's Bureau of Programs and Standards, said the government is setting an example for private industry by employing workers "without regard to age." He said that persons over 70 years of age often continue to work for the government, if they wish. There is no mandatory retirement age in government, he pointed out, adding that private industry might well follow suit.

Newell Brown, Assistant Secretary of Labor, said that one of the department's chief goals is to promote public understanding of the fact that there is no fixed age at which a person becomes too old to work and that each worker should be considered for employment on the basis of his individual qualifications as these measure up to the basic requirements of the job.

The general objective of the department's older worker program, he said, "is to help make it possible for older persons who desire and are able to work to continue their productive lives through suitable gainful employment."

Another witness before the subcommittee, Sen. Jacob K. Javits (R., N. Y.), said that discrimination against older workers "deprives the nation of a most important resource of experienced, often highly skilled employees, adds materially to the number of persons requiring public assistance, and deprives mature citizens of the dignity and status of self-support and continued participation in constructive economic activity."

Sen. Pat McNamara (D., Mich.), subcommittee chairman, remarked that "this barrier of age discrimination" is one of the chief issues before the subcommittee. He asked the witnesses whether the employment of older persons would reduce job

(Continued on next page)

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Riseman, J. E. F., *et al.*: Circulation 17:22, 1958

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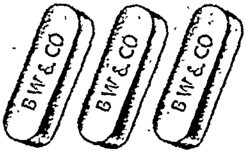


opportunities for younger persons. They said that there should be plenty of jobs for all in an expanding economy.

The subcommittee plans to hold hearings in at least six cities during the fall to hear local officials and representatives of interested organizations testify on problems in their areas.

CHAIRMEN NAMED FOR AGING CONFERENCE COMMITTEES

The chairmen of the 20 planning committees for the 1961 White House Conference on the Aging were appointed by Robert W. Kean, chairman of the advisory committee to the conference. The chairmen, all members of the 130-member advisory committee, met for an all-day session in Washington on July 30 to speed preparations for the conference.

"The planning committees have been established to cover the areas of major interests to the nation's increasing older population," said Kean.

Those named chairmen included Dr. Leonard W. Larson, Chairman of the American Medical Association's Board of Trustees, committee on health and medical care; Dr. Howard A. Rusk, Bellevue Medical Center, committee on rehabilitation; Dr. Ewald W. Bussey, Durham, N. C., committee on research in gerontology; Charles I. Schottland, former social security commissioner, committee on income maintenance and implications of inflation and other economic factors; the very Rev. Msgr. Raymond J. Gallagher, rabbi Marc H. Tannenbaum, and the Rev. William J. Villaume, co-chairmen, committee on religion; John B. Martin Jr., committee on population trends and social and economic implications; G. Warfield Hobbs, committee on impact of inflation on retired citizens; Dwight S. Sargent, committee on employment security and retirement; Joseph P. Anderson, committee on social service; Walter C. Nelson, committee on housing; George E. Davis, committee on education; Wilma Donahue, committee on role and training of professional personnel; Margaret A. Ireland, committee on family life, family relationships, and friends; Joseph Prendergast, committee on free time, recreation, voluntary services, and citizenship participation; Hardin B. Jones, committee on research in gerontology (biological); John E. Anderson, committee on research in gerontology (social science); Robert MacRae, committee on local community organization; Brevard Crihfield, committee on state organization; Viola Hymes, committee on national voluntary services and service organizations; and Harry G. Haskell Jr., committee on federal organizations and programs.

BLUE CROSS, BLUE SHIELD SUPPORT HEALTH INSURANCE BILL

Spokesman for the Blue Cross Association and Blue Shield Medical Care Plans asked Congress to approve a "long overdue" program of voluntary health insurance for civilian federal workers.

Testifying before the House Post Office and Civil Service Committee they endorsed, with minor changes, the legislation that cleared the Senate earlier this session.

"The nation's largest employer should aid its employees in securing needed health services," declared J. Douglas Colman, vice-president and secretary of Blue Cross. "The United States is the only large industrial nation in which personal health services are not a major governmental responsibility," he said, noting that "contributions to the cost of health service benefits is increasingly a standard part of the benefits offered by private employers with whom the federal government competes for competent personnel."

Dr. Donald Stubbs, chairman of the board of the national association of Blue Shield medical care plans, said health insurance "has become a condition of employment for a large segment of the population and in this respect the government has fallen behind the times by not helping to provide for the better health care of its employees."

Both officials recommended clarifying a section of the measure that authorizes the Civil Service Commission to approve, among other plans, "one governmentwide service benefit plan. . . ." Colman said that this might be interpreted as a requirement "to negotiate service contracts with physicians and hospitals in every city throughout the world where even one federal employee is located."

The American Medical Association, which also supports the bill, raised a similar objection to this provision.

The measure calls for the government to pay half the cost of the insurance, and gives the Civil Service Commission wide flexibility in establishing terms for the insurance. It would cost the government about 150 million dollars a year.

FLEMMING DEFENDS RELEASE POLICY

Arthur S. Flemming, Secretary of Health, Education, and Welfare, [illegible] a published charge that the department is misrepresenting government medical research achievements.

He said announcements should be made first in scientific journals, although in some important cases the department "has the responsibility" of simultaneously transmitting the information to the lay public.

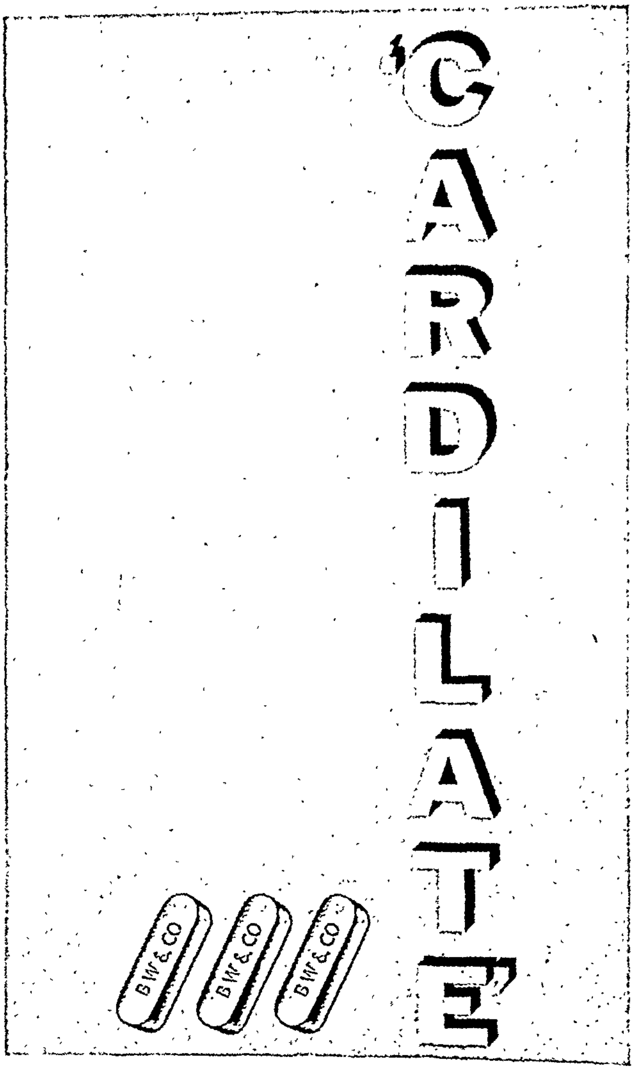
Flemming conceded that in one case the first sentence of a press release was "inadequate, in that it failed to indicate the extensive research, by both National Institutes of Health scientists and others, which, starting more than a decade ago, led to the results described in the release."

The first sentence of the release said, "Scientists at the National Institute of Mental Health have discovered the answers to one form of severe mental illness." The illness was phenylpyruvic oligophrenia.

Another disputed release started "Surgeon General Leroy E. Burney . . . announced today that a 'happy accident' of medical research has led to the discovery of a powerful new drug for treatment of gout. . . ."

Flemming said the release did not claim credit for NIH, and provided "full identification of the scientists, both in and out of government, and mentioned the institutions with which they were associated."

Asked at a news conference whether there might be any "political purpose" in the timing of news releases, often months after publication in scientific papers, Mr. Flemming said this was "certainly" not true. He said that he releases statements only when branches of HEW recommend that he do so.



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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

August

American Association of Electromyography and Electrodiagnosis, Mayo Clinic, Rochester, Minn., Aug. 29-30. Dr. Edward Lambert, Mayo Clinic, Rochester, Minn., Program Chairman.

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand R 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist cal Arts Bldg., Little Rock, Ark., Secretary.

Mississippi Valley Medical Society, Hotel Chase, St. Louis, Sept Oct. 1. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19 L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Exec Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surg Chicago, Sept. 13-17. For information write the Secretariat, 1516 L Shore Dr., Chicago 10.

Ohio Society of Anesthesiologists, Dayton Biltmore Hotel, Dayton, S 18-19. Dr. Nicholas G. DePiero, 9710 Garfield Blvd., Garfield 25, Ohio, Secretary.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 2 Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Exec Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 2 Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Te Chairman.

United States Section, International College of Surgeons, P House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake S Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake C Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Exec Secretary.

Western Neurosurgical Society, La Valencia Hotel, La Jolla, C Sept. 27-30. Dr. Ernest W. Mack, 505 S. Arlington Ave., Reno, Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Lo Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, C land, Oct. 15-17. For information write: Dr. Bertram B. Moss, 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 ond St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearbo Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Phi phia, Oct. 23-25. Dr. Philip Reichert, Empire State Bldg., New Y Executive Director.

American College of Chest Physicians, 25th Anniversary Hom ing Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Ko 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassado lantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Ph phia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., C Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hote Harbour, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolp Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray bent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Miami 33, Fla., Executive Secretary.

Association of Clinical Scientists, Sheraton-Park Hotel, Washi D. C., Oct. 10. Dr. Robert P. MacFate, 323 Northwood Rd., Riv Ill., Secretary-Treasurer.

(Continued on page 38)

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PSYCHOSOMATIC PROBLEMS IN A RAPIDLY GROWING SUBURB

Richard E. Gordon, M.D.
and
Katherine K. Gordon, B.S., Englewood, N. J.

Certain diseases were compared as to their incidence among patients admitted to general hospitals in three communities which differed markedly as to their rate of growth in recent years and as to the mobility of their inhabitants. Bronchopneumonia, representing disorders not psychosomatic in origin, was compared with duodenal ulcer and cardiovascular disease, representing tension disorders, and with asthma, considered as a parasympathetic psychosomatic disorder. In addition it was possible to compare figures obtained in 1958 with figures obtained in 1950. Asthma was more prevalent in the community with the highest percentage of older people. The tension disorders were most prevalent in the most rapidly growing suburban community. This finding agreed with results of previous studies of the distribution of emotional disorders among different groups within the communities.

MULTIPLE interrelated factors have been reported to be associated with psychosomatic disorders—genetic predisposition, body type and constitutional variables, early psychological conditioning, climate, diet, personality, occupation, exercise, and others. Recently, particularly in patients with coronary heart disease, important findings have been reported relating definite somatic abnormalities to behavior patterns and socioeconomic pressures and stresses.

Lee and Schneider[1] recently showed that lesser executives and white-collar workers were more prone to hypertension and arteriosclerosis than top executives. Friedman and Rosenman[2] reported their important findings that men exhibiting a behavior pattern primarily characterized by intense ambition, competitive "drive," preoccupation with "deadlines," and a sense of time urgency were more likely candidates for coronary artery disease than comparable groups of either more lackadaisical or chronically anxious and insecure, but noncompetitive, persons. American society praises and highly rewards competitive, "getting ahead" behavior. Such persons by their energy and drive, by working long hours, and by going to college at night often rise from working class, immigrant origins into the American middle class, buy their own homes, and move into the rapidly growing suburbs.

It would be interesting to learn whether incidences of coronary heart disease as well as several other psychosomatic disorders are rising in expand-

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ing suburban communities. For the rapidly changing community itself, with its higher taxes and overloaded schools, roads, recreational facilities, and other resources, may contribute its share of stress to a patient's overburdened psychophysiological functioning. Futhermore, this suburban move uproots all the family and places strains on the housewife[3] and her sons particularly that apparently interfere with their emotional health.

TABLE 1.—*Over-all Percentages of Various Disorders in Adults in Three Community Hospitals, 1956-1958*

	Englewood Hospital*	Kingston Hospital†	Olean General Hospital‡
Asthma	2.1	4.7	2.0
Coronary thrombosis	11.7	3.0	2.0
Essential hypertension	2.3	2.0	1.7
Hypertensive cardiovascular disease	12.0	3.2	5.0
Duodenal ulcer	9.6	7.1	2.8
Bronchopneumonia	7.3	5.3	5.0
Total no. of adult medical admissions	1,452	1,236	2,102

* In a rapidly growing suburb.
† In a moderate-growth community.
‡ In a slow-growth area.

Sociologists and social psychologists have for some time reported on the hazards of high-speed modern life, too rapid social mobility, and too reckless efforts at getting ahead and their relationship to family disorganization, divorce, delinquency, and emotional disorder.[4] Perhaps the rapid suburbanization of much of the American population is associated with attendant psychosomatic as well as emotional difficulties. If so, efforts at management and prevention cannot be directed at the individual patient alone—his personality, physical condition, and diet—but must also have family, industrial, and communitywide public health features.

Procedure of Study

Percentages of total medical admissions for asthma, coronary thrombosis, duodenal ulcer, essential hypertension, and hypertensive cardiovascular disease were obtained from three general hospitals, each in a community of different geographical mobility. The percentage incidence of bronchopneumonia in the three hospitals was used for comparison. The Englewood Hospital in Bergen County, New Jersey, represented a rapidly growing suburb; Kingston Hospital, Ulster County, New York, a moderate-growth, mixed-rural community; and Olean General Hospital, Cattaraugus County, New York, a stable rural area.

The problem was approached by several methods. *A comparison was made of percentages of the disorders* in admissions to all three hospitals in the year 1957. Olean General and Englewood were compared for relative change in gross percentages of these disorders from 1950 to 1958. Kingston and Englewood were compared for age and sex patterning of patients in 1957. Finally, possible change in age and sex patterning in Englewood Hospital during the period 1950-1958 was investigated.

Census data gave growth-rates as an indicant of geographical mobility. Previous studies have shown that rate of geographical mobility is highly correlated with cultural and socioeconomic mobility in Englewood and Bergen counties generally.[34] A sample of records of 97 Englewood Hospital adult patients, all under 60 years of age and admitted for psychosomatic disorders, gave marital status information (95% of men and 92% of women married).

It is hypothesized that differences in incidence of these psychosomatic disorders reflect differences in the social patterns in the communities the hospitals serve. It is assumed that modern diagnostic and therapeutic measures are reasonably constant in the medical practice of the several communities. Similarly, it is assumed that any change in percentages of psychosomatic disorders found in the periods under study is not greatly affected by any change in incidence of other disorders, such as a decrease in bacterial infection due to more effective antibiotics.

Results

Asthma.—For asthma, over-all incidence was lower in Englewood than in Kingston Hospital (x^2 [chi square]=23, $p < 0.001$) but slightly higher than in Olean (table 1). As with every other disorder, however, percentages of young women with asthma (ages 18 to 44) were higher in Englewood than in Kingston, but not significantly so (table 3).

Coronary Thrombosis.—Incidence of coronary thrombosis was much higher in Englewood than in Kingston or Olean hospitals in 1957. The percentage has risen in both rural and suburban hospitals since 1950 (table 2). (Comparing Englewood with Olean Hospital in 1957, x^2=130, $p < 0.001$; Englewood 1950-1952 versus 1953-1958, x^2=10.3, p near 0.001). The incidence of coronary thrombosis in younger men rose, but not significantly, in Englewood from 1950 to 1958 (table 4).

Duodenal Ulcer.—Incidence of duodenal ulcer was again much higher in Englewood than in Kingston, even more so than in Olean (x^2=75, $p < 0.001$ [table 1]). But there has been only a slight increase in over-all incidence in Englewood (table 2), again associated with a rise in number of young women (table 4).

TABLE 2.—*Change in Over-all Percentages of Various Disorders in Englewood and Olean Hospitals, 1950-1958*

	Coronary Thrombosis		Duodenal Ulcer		Essential Hypertension		Hypertensive Cardiovascular Disease		Bronchopneumonia	
	Englewood	Olean	Englewood	Olean	Englewood	Olean	Englewood	Olean	Englewood	Olean
1950-1952	8.5	2.1	4.5	1.7	2.0	1.4	13.5	5.8	5.4	4.8
1953-1955	14.3	2.9	4.5	2.1	3.0	1.1	18.0	4.1	6.1	4.4
1956-1958	12.5	2.7	4.7	1.9	2.4	1.3	12.0	5.0	7.4	5.0

Much higher percentages of women had duodenal ulcer in Englewood than in Kingston Hospital (for all women, x^2=7.9, $p < 0.01$; for young women, x^2=5.8, $p < 0.02$ [table 3]). Since 1950 the incidence of duodenal ulcer in women of all age groups has risen in Englewood ($\chi^2=3.7$, p near 0.05), but particularly that in young women ($\chi^2=4.2$, $p<0.05$).

Essential Hypertension and Hypertensive Cardiovascular Disease.—Englewood's incidence of essential hypertension and hypertensive cardiovascular disease was significantly higher than that of Kingston ($\chi^2=4.7$, $p<0.05$) and very significantly higher than Olean's ($\chi^2=45$, $p<0.001$) (table 1). There was a rise in Englewood in essential hypertension from 1950 to the present ($\chi^2=3.1$, p near 0.05), but not in Olean (table 2). The percentage of young women with hypertension was also greater in Englewood than in Kingston, but not significantly (table 3). A rise in incidence of essential hypertension from 9% to 15% occurred from 1950 to 1958 in Englewood (table 4), but not to statistically significant levels.

TABLE 3.—*Patterning of Various Disorders, Comparing Englewood and Kingston Hospitals, 1956-1958*

	Asthma				Coronary Thrombosis				Duodenal Ulcer				Essential Hypertension				Bronchopneumonia			
	Englewood		Kingston		Englewood		Kingston		Englewood		Kingston		Englewood		Kingston		Englewood		Kingston	
Age Group, Yr.	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F
18-44	13	26	6	20	9	1	6	0	19	13	30	7	4	8	6	2	6	15	14	12
45-59	12	16	19	14	26	4	29	2	27	8	26	3	14	11	6	12	15	12	17	10
% younger	67		60		40		37		67		66		37		26		48		53	
60-69	14	6	10	12	17	11	24	16	20	13	13	8	9	25	14	19	13	9	10	5
70 or older	7	6	13	5	15	17	10	13			9	4	9	20	14	26	15	14	21	11
% older	33		40		60		63		33		34		63		74		52		47	
Total																				
%	46	54	49	51	67	33	69	31	66	34	78	22	36	64	41	59	49	51	62	38
No.	86		82		207		38		222		88		107		64		211		66	

Bronchopneumonia.—The over-all percentage of bronchopneumonia in the three community hospitals was not very much different in the year 1957 (table 1) and was relatively unchanged through the years in Olean (table 2). However, two consistent trends appear, for higher percentages in boys and young women patients in Englewood in recent years as compared both to the other hospitals and to previous years in the Englewood Hospital (tables 3 and 4). These differences are statistically significant. (For young men versus young women in Englewood Hospital, comparing 1950-1952 and 1956-1958, $\chi^2=5.4$, $p<0.02$; young men versus young women, Englewood and Kingston hospitals, 1957, $\chi^2=4.0$, $p<0.05$; boys versus girls, Englewood Hospital, 1950-1952 and 1956-1958, $\chi^2=3.4$, p near 0.05; and boys versus girls, Englewood and Kingston hospitals, 1957, $\chi^2=4.7$, $p<0.05$).

TABLE 4.—*Patterning of Various Disorders, Englewood Hospital, 1950-1958*

	Coronary Thrombosis						Duodenal Ulcer					
	1950-1952		1953-1955		1956-1958		1950-1952		1953-1955		1956-1958	
Age Group, Yr.	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F
18-44	6	0	5	1	8	1	28	7	29	8	20	13
45-59	37	7	30	5	27	4	31	10	23	14	27	8
% younger	50		41		40		76		73		67	
60-69	21	10	24	10	16	12	17	7	18	9	20	12
70 or older	12	8	11	14	15	15						
% older	50		59		60		24		27		33	
Total												
%	76	24	70	30	68	32	76	24	70	30	67	33
No.	186		332		361		98		134		160	

	Essential Hypertension						Bronchopneumonia					
	1950-1952		1953-1955		1956-1958		1950-1952		1953-1955		1956-1958	
Age Group, Yr.	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F	%M	%F
18-44	7	9	5	11	6	15	13	10	8	10	6	14
45-59	11	25	16	13	18	18	11	10	13	15	15	13
% younger	52		45		57		44		46		48	
60-69	9	23	9	19	3	22	9	12	12	11	13	9
70 or older	4	12	7	20	8	10	19	16	5	16	15	14
% older	48		55		43		56		54		52	
Total												
%	31	69	36	64	35	65	52	48	47	53	49	51
No.	56		82		161		126		172		211	

Comment

Relationship of Degree of Mobility and Percentage of Psychosomatic Disorders.—It would appear that, except for asthma, there was a direct and very significant relationship between the degree of mobility of the community and the percentages of the several psychosomatic disorders studied. Englewood Hospital, in a fast-growing suburb, had the highest percentages of patients with coronary thrombosis, duodenal ulcer, essential hypertension, and hypertensive cardiovascular disease; Kingston Hospital was intermediate; and Olean General Hospital, in a stable rural community of western New York state, had the lowest incidence (table 1).

It seems that, with the rapid growth of the suburban area around Englewood since 1950, percentages of coronary thrombosis and hypertension have increased more rapidly. In Olean Hospital, in a rural community, only the percentage of coronary thrombosis increased. Interestingly, incidence of bronchopneumonia also increased in Englewood, primarily because of the greater number of boy and young women patients (table 2).

For every disorder in Englewood Hospital percentages of young women patients (between 18 and 44 years of age) exceeded those in Kingston

Hospital, most particularly for hypertension and ulcer. Generally women of all ages were more frequently patients with psychosomatic disorders in Englewood than in Kingston, but this was largely due to the preponderance of the young group in the population. Of these women, 92% were married. Moreover, relative percentages of women patients with coronary thrombosis and duodenal ulcer have increased in Englewood Hospital.

More older persons were patients with every psychosomatic disorder in Kingston than in Englewood Hospital. However, percentage-wise, more older persons in Englewood were patients with bronchopneumonia, the nonpsychosomatic disorder used for comparison. (The greater general incidence of elderly patients with psychosomatic disorders in Kingston Hospital is not surprising, as that community has a larger older population, estimated from the 1950 census as about 1.4 times as many persons past 60 years of age as in the Englewood area.) Comparable mobilities, with migration rates calculated from the 1950 census used as an index and supported by subsequent interim census reports, indicate that the average annual migration rate for Bergen County has been about 7%, for Ulster County about 5%, and for Cattaraugas 4%.

It seemed that rapid social mobility was related not only to emotional difficulties but also to a rising incidence of tension-related psychosomatic disorders. Such disorders as coronary thrombosis, duodenal ulcer, essential hypertension, and hypertensive cardiovascular disease were more prevalent in the rapidly growing mobile communities and less so in the more slow-growing, stable one. The incidence paralleled the degree of mobility. It seems that divorce and suicide rates also follow this pattern, and this is presently under further investigation.

Not only were there differences between more and less mobile communities, but within the same more mobile county the incidence of coronary thrombosis and hypertension rose in the period of rapid community growth and expansion—1950-1958. Incidence of coronary thrombosis also rose in the more stable comparison community, suggesting that we are observing a large-scale problem, more prevalent in, but not limited to, the rapidly growing areas of the country and associated with the national increase in mobility since World War II.

In this study, as well as others, it was apparent that, although all groups presently have more difficulties, the young married women were relatively more prone to react with psychosomatic disorders and other emotional difficulties than other adult groups in the mobile communities. Boys seemed to suffer more than girls. The elderly were having greater difficulties in the rural areas where emigration, rather than immigration, is the main form of geographical mobility.

One cannot assume a causal relationship between mobility and over-all rise in incidence of psychosomatic disorders seen in a suburban hospital, for an argument can be documented that the emotionally unstable are more mobile than the emotionally stable and that the potentially hypertensive or ulcerous will be more mobile. But it is harder to show why married women and sons, whose rates are rising, were more unstable than the men, when much of geographical mobility frequently is related to husbands' new job opportunities. The wives and sons are sometimes reluctant travelers. There is plenty of evidence that the marginally adjusted persons who have constitutional susceptibilities, and who have been sensitized by unfortunate early life experiences, become psychiatric and psychosomatic patients more often. Perhaps this mobility increases the strains on their already heavily taxed systems to the point of illness. Thus there seems to be a circular causal relationship. But in a small percentage of cases there is no history of major predisposition.

One disease, asthma, was more prevalent in the rural community. This illness is not a tension disorder but a parasympathetic psychosomatic disorder, closely associated with emotional depression and "unresolved dependence."[5] It occurred more frequently in Kingston Hospital in the heart of the Hudson Valley, which is noted for respiratory ailments and which is a community with many lonesome elderly people. A high incidence was found in the older members of the population. They are being left behind there, are without adequate activities, and are often quite depressed.

Change in Social Role of Married Women.—Married women are undergoing a long-term change in social role in the United States as a result of greater economic, political, and educational opportunity. This opportunity brings with it expectations for greater independence and assumption of responsibility.

Traditionally, and particularly in the more restrictive ethnic groups, into which many of the Bergen County women were born, women were protected and kept dependent but were provided much help and honor in their homemaking and child-rearing role by the other members of the family. With the disruption of big multigeneration family living and the moving of married women away from their parental homes and neighborhoods, in the present American pattern, many women are exposed to responsibilities for which they are poorly prepared, and for which they receive little assistance, guidance, relief, and relatively less recognition and praise.

They have not learned the techniques of considerate self-assertiveness necessary to making friends, of competition, and of realistic independence. They are shy, unassertive, and insecure. An unrealistic precarious "pseudoindependence" is thrust on them. The other women in the community are often similarly strained, and are often from different religious, ethnic, and cultural backgrounds. Communication and mutual assistance thus do not readily take place. Husbands do not understand the problem either and are themselves working long hours, fulfilling their business responsibilities. They are often chagrined at their wives' complaints but are not very encouraging, respecting, praising, or helpful with "women's work."

Some women, often similarly protected and restricted in early life, have also acquired intellectual, social, business and professional, and artistic interests and tastes as a result of their educations and backgrounds which often go frustrated in the housewife's daily routine. The woman who constitutionally or genetically was endowed with a sensitive stomach, and who may have undergone some early conditioning through unpleasant experiences with food and eating, may develop an ulcer in a continuing atmosphere of anxiety, chronic tension, frustration, and confusion which she cannot comprehend and relieve. She may perhaps be particularly susceptible, if she has acquired the temperament described by Friedman and Rosenman, and drives herself compulsively to maintain a meticulously clean house, meanwhile meeting schedule deadlines—chauffeuring husband to and from the commuter train and children to and from school, preparing meals, and so forth.

Under these circumstances of increased demands and expectations of poorly prepared women, with attendant rise in their rates of situational emotional maladjustments and other psychiatric disorders, and in psychosomatic reactions, are we observing the beginnings of an equalizing of the morbidity rates of the sexes? In the 19th century ulcer was more prevalent in women than in men, as it is at present.[6] Already in Englewood Hospital 40% of ulcer cases in young adults occur in women. Even the incidence of bronchopneumonia is rising with them, for young women without family and friends to rely on, and who cannot afford paid help, cannot go to bed with a bad cold but must care for their preschool children, shop, and continue "on the job" —until they are laid low by pneumonia. It seems apparent that any attempt to relieve the tensions related to psychosomatic disease must take into consideration the needs of wives and children, as well as husbands, all of whom may suffer.

Assumption of and Preparation for Responsibility in Men.—Let us consider further the problem of assumption of and preparation for responsibility with regard to men. Lee and Schneider's[1] very interesting paper on hypertension and arteriosclerosis in executives showed that top executives had less of these disorders than the lesser executives and white-collar workers. This finding is not surprising when we consider some of the sociodynamics and psychodynamics.

Is it responsibility alone that leads to emotional strain? Many top executives have had excellent preparation for responsibility, through upper-middle-class and upper-class birth, good education, and guidance and assistance while they were young by family and friends who themselves were experienced top executives. They do not necessarily feel "the strains of executive responsibility" too severely. The making of decisions does not of necessity provoke anxiety and tension. It is the possibly deleterious consequences to the decision maker of a wrong decision which may cause him anxiety and grief.

The person who has been sensitized by stresses in early life may be far more susceptible to emotional and psychosomatic disorders. He may have come from a home in which his father was out of work during the Depression and took to drink, in which the parents were immigrants and could not prepare him well for adjustment to the American culture, or in which parents were separated, divorced, or widowed. This person, if exposed to the realistic strains of upward mobility, is more likely to develop an emotional and/or psychophysiological disturbance in adult life. He is usually not a top executive; he has not come that far yet. He is struggling upward out of the working class into subexecutive white-collar jobs and lesser managerial positions for a secure, more stimulating, and interesting life, and in order that he will not be thrown back into an often hungry, or stultifying, or degraded position in a culture that recognizes the man who gets ahead and scorns the failure. The recent-generation American, the night school scholar, the man from the minority ethnic or religious group, the struggling rapidly upwardly (and against downwardly) mobile person is more likely to be the potential psychiatric or psychosomatic patient. He usually has no close and loving experienced parent to guide him in his decisions. He must learn everything the hard way—by personal trial and success or error. The upwardly mobile person may have a great deal to lose and knows it well. If his decision backfires he may lose his job and his future and be thrown back to the insecurities of his past. He wears his responsibilities heavily.

The financially and socially well-to-do and well-born person has usually been burned less in his early years and is often well established so that he cannot be much hurt if he makes a bad decision once in a while. He has not much to fear from the past, present, or future so can relax at the end of the day, can exercise, look after his health, and play. Often (but not always) our top executives are born to their class. They carry more responsibility, but they have had better preparation and less to fear and dread. The lesser executives and nonexecutive white-collar groups have usually risen to their positions from humbler origins. Our Englewood and Bergen County new residents, and particularly our psychiatric patients, are largely drawn from the latter groups.[7] One wonders whether physicians, too, who also have a higher mortality from heart disease,[8] are not in large part from similar socioeconomic situations.

The upwardly mobile are often fiercely competitive, "driving," and excitable in their effort to continue to strive upward and to keep from being crushed back down. Their physiological mechanisms for coping with both acute and chronic stress are already overtaxed. They themselves are pushed and they are continually struggling with each other for a place at the top. Hollingshead and Redlich[9] have shown that the top echelon of the upper class insulate themselves from the upwardly striving and make it not at all easy for the latter to rise. They have already arrived and naturally protect themselves from the unpleasant aggressiveness and competitiveness of the climbers struggling upward. Thus the upwardly mobile usually must compete most of the way for greater security and an enjoyable rewarding life. In the mobile suburbs they are the majority. All struggling together, they compete with each other. They provoke discomforts for each other in home, office, and on the highway, and they recondition each other's emotional-psychophysiological disturbances. This type of person will only stop when he feels that he has found a really secure and interesting place for himself and can settle back, feeling well protected, and begin to relax and enjoy living. When the memories of his past are no longer supported by present dangers, his anxiety and tension can subside. However, he still has to learn to play, for most of his education has been for work, not for constructive leisure, and perhaps by this time irreversible anatomic damage already may have occurred to his system.

His wife will relax after she also has learned greater skill, efficiency, and confidence in coping with her new and difficult responsibilities and when she has found helpful assistants, helpers, and advisers among her family and new neighbors and in her husband. She, as well as her husband, once she has the security of fulfilling her responsibilities comfortably, must still learn better to enjoy her freedom, independence, and leisure constructively. The psychophysiological mechanism of reciprocal inhibition will then operate. The person who is enjoying himself does not experience emotional tension symptoms readily.

The Father-Son Problem.—As to the father-son problem, the modern middle-class father's work and leisure are geared toward his individual economic success. His son contributes little to this, in contrast to a farmer's or blacksmith's son. On the contrary, children interfere with personal advancement as well as freedom. The cost of their education represents an increasingly greater threat to the father's financial security. Children interfere with husband and wife companionship and personal leisure. Fathers, sensing their sons' needs, but having little in common that is mutually profitable, may try to play with sons on the latters' level. This is done partly out of a sense of obligation and compulsion and, needless to say, is not as wholesome as if it arose out of larger common goals.[10]

Conspicuous Consumption.—Many of our patients are overconcerned about keeping up appearances: a new car every few years is to them almost a necessity, there cannot be a blade of crabgrass in the lawn, the house must be spotless and dustless, the children must be kept scrubbed clean. For the already overstrained couple, "conspicuous consumption" can help cause bad tempers and high blood pressure.

Effectiveness of Insight in Psychotherapy.—A word of caution: only if a person's difficulties are entirely in the past, and his present is devoid of realistic anxiety-producing and tension-producing dangers, can he "take hold of himself," "slow down," and "stop worrying"—and then not always. He usually must be shown why he is under tension and that the strain is now over. This is the essence of the effectiveness of insight in psychotherapy. Our autonomic nervous system functions as its name indicates—automatically—it is not under conscious control. We cannot will it to "calm down." It reacts reflexly to actual events in our present lives or reminders of stressful events from the past (conditioned stimuli) which indicate possible potential danger. Injunctions to "stop pushing yourself or you'll have a heart attack" may even add a new fearful stress unless practical suggestions are offered as to the means by which life can be made much easier and more realistically secure. A pattern of behavior, both psychological and psychophysiological, can be changed, but only after removal of real objective difficulties—"traumas," "stresses," "strains," psychological or physical injuries—dangers that are both conditioned and unconditioned stimuli for evoking the behavior.

Once the real situation has improved, a calming down can occur. However, a psychosomatic or emotional disorder is itself a stress, and a disgrace in our society's thinking. The fears of patients with psychophysiological symptoms, whether with organic lesions or not, are increased by the very presence of the symptoms. They have seen friends and relatives succumb to emotional disorder, heart attacks, or early death. They are thus prone to dread these consequences. This new worry itself, conditioned to real occurrences in their lives, exacerbates their disorders. Thus personal and social strains in their lives arouse tension, make for fears, and contribute to psychophysiological disorders. Then the symptoms of the disorder add to the fears and a vicious cycle is under way.

Thus we help our patients not by frightening injunctions but by clear explanations of how their symptoms and disorders came about, the physiological mechanisms, personality factors, and social and economic problems. Understanding is reassuring and can lead to intelligent action. Further guidance as to the method of reducing the stresses and strains —the dangers and difficulties in their lives—may permit a calming down and gradual extinction of the reversible part of their psychophysiological reactions. This approach is most important and will be further elaborated in the following section.

Treatment, Rehabilitation, and Prevention.—Investigation of the many factors correlated with various psychosomatic disorders ultimately leads to better treatment and control. A series of studies of emotional disorder associated with pregnancy and childbearing[11] has helped develop an apparently useful program of preventing or ameliorating postpartum emotional difficulties at the Englewood Hospital. A technique useful in alleviating these acute and usually short-lived puerperal disorders may not be exactly applicable to chronic psychosomatic disorders, but the method of investigation possibly may serve as a model with other illnesses.

In brief, this method was as follows. First, the life histories were studied of four groups of women: (1) those who suffered postpartum psychiatric disorders, (2) those who suffered milder postpartum upsets but who were managed without psychiatric help, (3) normal new mothers, and (4) married women of the same age who suffered psychiatric disorders unassociated with pregnancy.

First, the stressful life history features which separated the various groups were identified. Second, a prediction scale of significant life history items was developed and tested on new series of new mothers. It was found to identify in the aggregate the subsequently emotionally upset. Third, study of items correlated with emotional upset and their intercorrelations with each other led to development of hypotheses as to dynamics of the disorders. Fourth, a set of instructions to expectant parents was developed from these hypotheses which pointed to some of the potential dangers and suggested means of modifying the situation. This was put to test with quite successful results with the experimental as compared to the control groups of subjects. Fifth, responses of the subjects in relation to the recommendations of the instructions were measured and their intercorrelations with each other obtained. These are now leading to further improvements in the instructions.

A possible investigation of cardiac disorders, perhaps leading to improved rehabilitation and prevention, is now being planned at the Englewood Hospital, with this experimental design used as a model. It was hypothesized that the apparent success with postpartum patients was related to a method of instruction which demonstrated the realistic and practical steps to take to reduce stresses and strains that demonstrably precipitate emotional difficulties. Less may possibly be done in reducing the effect of early childhood sensitization and conditioning to emotional and psychosomatic disorders. But the previous study seemed to indicate that only two 40-minute classroom sessions of instruction in antenatal classes were quite effective in helping subjects make the necessary changes in their lives prior to delivery and in preventing postpartum emotional difficulties from developing. Perhaps increasing study of the important environmental stresses that precipitate other psychosomatic conditions, particularly coronary artery disease, in conjunction with many other approaches, may help develop practical information which will be useful in prevention, treatment, and rehabilitation.

Summary

Investigation was made of the comparative overall incidences of asthma, coronary thrombosis, duodenal ulcer, essential hypertension, and hypertensive cardiovascular disease in several communities which differ in mobility. The age distribution, sex pattern in 1957, and the change in pattern from 1950 to 1958 were also obtained. Bronchopneumonia was used as a comparison disorder.

Tension disorders were most prevalent in a rapidly growing suburban community and least prevalent in a stable rural area. Differences in incidence were highest and incidence rose the most in young married women in the period of rapid growth in the suburb. Asthma was more prevalent in Kingston, a community of many older people. Generally, older people had more psychosomatic illness in stable rural areas and younger persons had more in the growing suburb. The data support those found in other investigations of psychiatric inpatients and outpatients.

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SOME PSYCHOSOMATIC ASPECTS OF ASTHMA

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The validity of the hypothesis that asthma is a psychosomatic disease was tested in a study of 44 patients with bronchial asthma, 15 with allergic rhinitis, and 9 with pulmonary emphysema. All patients took the short form of the Minnesota Multiphasic Personality Inventory (MMPI). When the asthmatics were classified as to the severity of their dyspnea, a correlation was found indicating that the scales for hypochondriasis, depression, and hysteria reflected some variable related to the functional classification of the asthma. No comparable correlation was found with the amount of medication taken by the patient or the duration of the asthma. Asthma could be called a psychosomatic disease, but the possibility that some of the scores in the MMPI may actually be a more direct measure of symptoms requires further investigation.

Laennec was the first to propose that asthma is a neurosis dependent on either a functional or an organic change in the nerve centers.[1] This hypothesis has received increasing support until the present time, so that asthma is considered by some[2] to be a classic example of a psychosomatic disease.

Reports to date of the psychological traits considered characteristic of patients with asthma have, however, been conflicting. This conflict possibly results from variable diagnostic criteria for asthma, sampling of the asthma population, and psychological investigative techniques utilized.

One of the most widely used psychometric tools has been the Minnesota Multiphasic Personality Inventory (MMPI). It has been extensively investigated with respect to factor loading, reliability, and validity of the whole test and individual scales. Because of the literature available defining the limitations of this test,[3] it was thought that it might be of aid in the psychological study of a medically well-defined population of asthma patients.

If there is validity to the hypothesis that asthma is a psychosomatic disease, then analysis of the data obtained by a test that purportedly detects the psychological traits characteristic of such a disease should demonstrate these to be present to a significant degree in a group of patients with asthma.

Method

The MMPI scales were constructed by comparing the responses of patients with established psychiatric diagnoses with those of persons not under psychiatric care; these were termed as follows: hypochondriasis (Hs), depression (D), hysteria (Hy), psychopathic personality (Pd), paranoia (Pa), psychasthenia (Pt), masculinity-femininity of interest (Mf), schizophrenia (Sc), and hypomanic trends (Ma). The lie score (L) and validity score (F) are for determining the patient's understanding, cooperativeness, and tendency to place himself in a favorable light. The K scale is designed to increase the discriminatory value of the Hs, Pd, Pt, Sc, and Ma scales.[4]

The group studied consisted of 44 patients with bronchial asthma, 15 patients with allergic rhinitis, and 9 patients with pulmonary emphysema. All

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were selected in sequence from the patients seen in the Long Beach Veterans Administration Hospital allergy clinic during a three-month period.

The diagnosis was established by the characteristic symptoms, physical findings, laboratory data, and skin reactions to allergens thought to be consistent with the patient's history. This limited the patients of the asthma group to those with a relatively well-defined allergic condition, and it is believed that no patients were included with significant pulmonary emphysema, bronchiectasis, congestive heart failure, or neurotic hyperventilation. The group with allergic rhinitis included no patients with evidence of such complications as deviated nasal septum or purulent sinusitis.

All patients with asthma and allergic rhinitis had been observed at weekly intervals for purposes of a therapy investigation for at least six months and had been carefully evaluated and classified on the basis of functional ability. The nine patients with pulmonary emphysema were selected in sequence from a group referred to the clinic because of dyspnea and wheezing. Their true diagnosis was established on the basis of pulmonary function studies and exclusion of asthma by absence of the characteristic history, symptoms, and significant skin reactions to allergens.

All patients were given the short form[5] of the MMPI and were allowed to complete it without time limitation. Absolute scores on the various scales were converted to standard score (TorTc scale) for purposes of comparison.

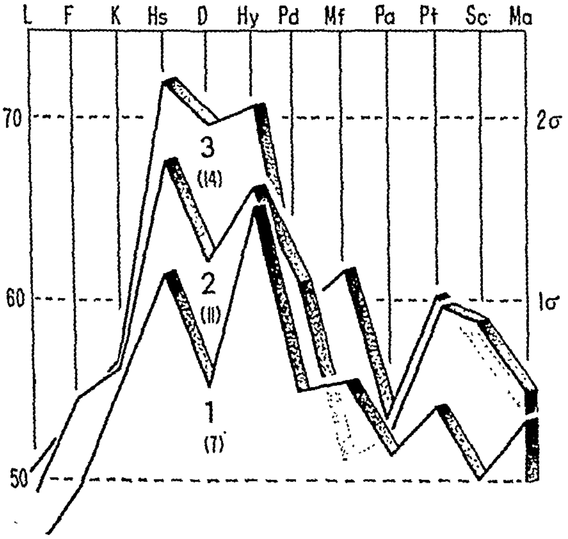

Fig. 1.—MMPI profiles of patients with asthma, functional classes 1, 2, and 3.

Results

The resultant mean profiles were determined for the subgroups of patients with allergic rhinitis, asthma, and pulmonary emphysema. The patients with asthma were arbitrarily subclassified into five groups at the time of testing on the basis of functional ability according to the following criteria as applied to the three-month period prior to testing: 1. The patient had definitely established asthma at some time in the past but no significant paroxysms. 2. The patient had occasional episodes of wheezing and dyspnea but not severe enough to require continued medication or interfere with sleep, daily activities, or regular work. 3. The patient had frequent paroxysms of wheezing and dyspnea severe enough to require medication at least weekly, causing occasional loss of sleep, occasional interference with daily activities, but less than one week's work loss due to asthma. 4. The patient had daily paroxysms of wheezing and dyspnea requiring regular medication, with moderate to marked interference with daily activities, and causing from one to three weeks' work loss due to asthma. 5. The patient had daily to continuous wheezing and dyspnea requiring constant medication, over two weeks' hospitalization for asthma, or over three weeks' loss of work due to asthma.

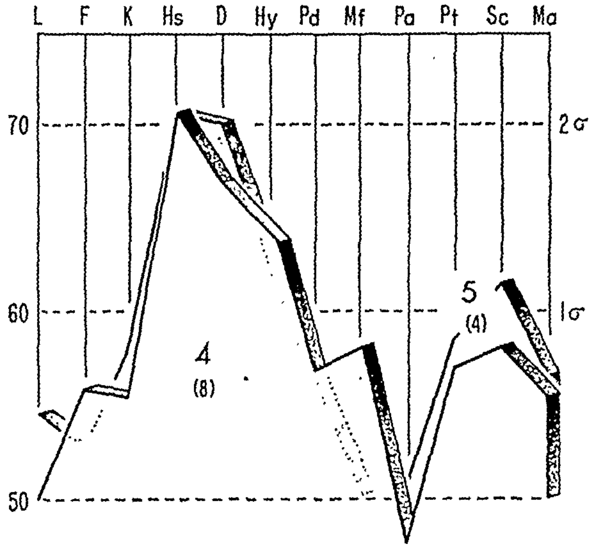

Fig. 2.—MMPI profiles of patients with asthma, functional classes 4 and 5.

Mean scores for patients with asthma in the various functional classes are shown in figures 1, 2, and 3. It is evident that those with asthma in functional class 1 show the so-called psychosomatic V (characteristic relationship of high scores for Hs, D, and Hy scales), with classes 2 and 3 showing progressively greater increases in these scores and retaining the same relative quantitative relationship among them. Classes 4 and 5 show no further increase in the Hs and D scores over those of class 3 but do show a relative decrease in the Hy score, with consequent disappearance of the psychosomatic V. (This phenomenon has been called "somatization" and is said to be a characteristic modification of the "conversion V" when an "organic," as opposed to a "functional," cause for symptoms is present.)

In order to compare the area of the psychosomatic V present in the different functional classes of asthma, the score $(\frac{Hs+Hy}{2})$—D was computed (see table) and compared to the functional class. There appears to be a close negative correlation between increasing functional impairment by group and the area of the psychosomatic V shown in the mean profiles. (The score $\frac{Hs+D+Hy}{3}$ has been said to be a measure of anxiety[6] and shows less correlation with degree of functional impairment than does the psychosomatic V.) These data would indicate that the Hs, D, and Hy scales and their interrelationships effectively reflect some variable related to the functional classification of asthma.

*Average Scores for Hs, D, Hy, Psychosomatic V, and Anxiety Scales for Patients with Allergic Rhinitis, Asthma, and Pulmonary Emphysema**

	MMPI Scales							Psychosomatic V, $\frac{Hs+Hy}{2}$—D	Anxiety, $\frac{Hs+Hy+D}{3}$
	Hs		Hy		$\frac{Hs+Hy}{2}$	D			
Group (No. of Patients)	Av.	S.D.†	Av.	S.D.		Av.	S.D.		
Allergic Rhinitis (15)	62.7	10.9	61.7	12.1	62.2	59.8	11.0	2.4	61.4
Asthma, functional class									
1 (7)	61.5	12.3	65.1	10.5	63.3	55.1	8.1	8.2	60.6
2 (11)	67.6	12.7	66.2	9.0	66.9	63.5	10.0	3.4	65.8
3 (14)	71.9	13.8	70.5	8.5	71.2	69.5	8.6	1.7	70.6
4 (8)	70.5	11.3	63.7	12.0	67.1	66.8	12.0	0.3	67.0
5 (4)	70.5	18.5	61.2	15.0	65.8	70.0	12.8	—4.2	67.2
Pulmonary emphysema (9)	82.8	18.0	73.1	9.7	75.8	71.5	11.5	4.3	77.9

* Hs = hypochondriasis, D = depression, Hy = hysteria.

† S.D. = standard deviation.

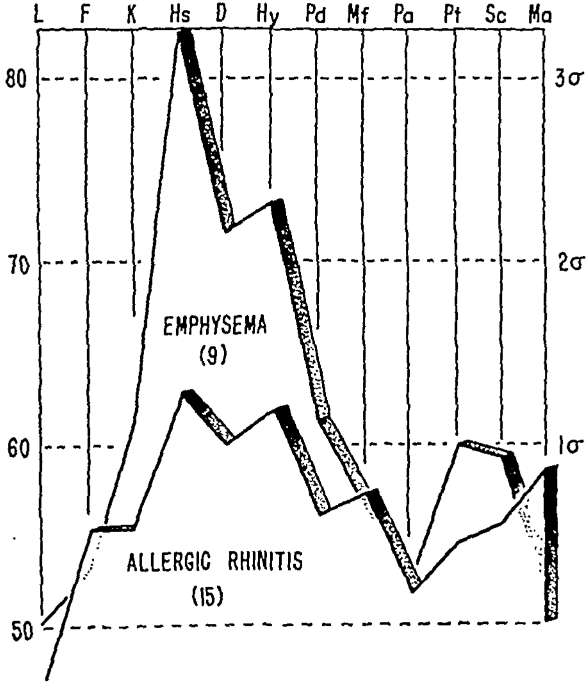

Fig. 3.—MMPI profiles of patients with allergic rhinitis and pulmonary emphysema.

The group with pulmonary emphysema showed a profile with the greatest deviation from the normal mean (fig. 3) but it still retained a definite similiarity to profiles of the first three functional classes of asthma so far as the Hs, D, and Hy scales were concerned. The group with allergic rhinitis had a profile which also resembled those in the first three functional classes of asthma, particularly functional class 1, in which the patients had been asymptomatic for three months prior to taking the test.

Since patients with asthma have a functional capacity at least partially dependent on the amount of medication they receive, they were also arbitrarily subclassified on the basis of therapy received according to the following criteria, as applied to the three-month period prior to testing: 1. The patient needed and took no medication. 2. The patient took only occasional doses of sympathomimetic drugs orally. 3. The patient regularly took sympathomimetic drugs orally, with occasional, but not regular, use of sympathomimetic nebulization or aminophylline suppositories. 4. The patient regularly took sympathomimetic drugs orally, used sympathomimetic nebulization daily, and received epinephrine injections not more than once weekly. 5. The patient took any or all of the above medicaments but received an average of more than one epinephrine injection weekly or was on long-term steroid medication. There appeared to be no significant correlations between MMPI scores and therapeutic classification.

Patients were also classified into four groups according to duration of their asthma, and the mean scores were computed. Again, there appeared to be no significant correlation between this factor and the MMPI scores.

Comment

It is evident that patients with asthma show an MMPI profile with characteristically high scores for the Hs, D, and Hy scales, in a relationship which has been called the psychosomatic V. On the basis of this consistent finding asthma could, therefore, be called a "psychosomatic" disease. It is further evident from these data that the closest correlation of this phenomenon is found to be with the degree of the patient's functional impairment or the severity of his illness. Patients with allergic rhinitis, who were comparatively unimpaired in relation to significant interference with sleep, daily activities, and ability to work, showed a profile similar to that of patients with asthma in functional class 1, who were also comparatively unaffected by their disease during the three months prior to testing. The remaining functional classes of patients with asthma showed increasing scores on these scales as the degree of functional impairment increased. The patient with pulmonary emphysema, with no evident allergic disease but with similar symptoms and even greater functional impairment than the patients with asthma, showed the greatest increase in these scores (and could also be said to have a psychosomatic disease).

All objective supportive evidence, including positive family history of allergy, associated allergic stigmata such as urticaria and allergic dermatitis, and number and intensity of positive skin reactions to allergens, indicated that the patients with allergic rhinitis were equally as "allergic" as the patients with asthma. The patients with pulmonary emphysema had no demonstrable allergy. If these groups are arranged in a continuum from the one having no significant functional impairment to the one most severely impaired, it is evident that the degree of profile deviation from the normal mean is more closely correlated with symptom severity than presence of allergic disease. It is further evident that, in the patients with asthma, the psychosomatic pattern of the profile progressively decreases as symptom severity increases.

It is possible that this unexpectedly close correlation between the patient's symptom severity and type of MMPI profile may arise from anxiety over symptoms. It has been suggested that the Hs, D, and Hy scores will serve as a rough measure of anxiety.[6] The mean anxiety scores for the groups studied are given in the table. It is evident that this score does not show so close a relationship to functional impairment as does the psychosomatic V.

An alternative explanation of some of this correlation is that a portion of the Hs, D, and Hy scores may actually be a more direct measure of symptoms. This hypothesis is currently under investigation. Complete determination of the factors responsible for these scores in patients with asthma will be evident from an item analysis of these responses, as well as other psychometric and projective techniques presently in use in this clinic to investigate the psychological traits of the patient with asthma.

Summary

Study of a well-defined population with bronchial asthma with use of a well-known psychometric tool, the Minnesota Multiphasic Personality Inventory (MMPI), indicated that the "psychosomatic" profile is more closely correlated with the degree of functional impairment than the presence or absence of allergic disease.

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Mrs. Elsie Carruthers and Miss Arden Knaak assisted in test administration, scoring, and data compilation.

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STAPHYLOCOCCI WITHIN PHAGOCYTIC CELLS.—Some years ago we noted that pathogenic staphylococci were steadily ingested by human leukocytes in systems in which other virulent microbes failed to be phagocytosed. Despite the fact that virtually all staphylococci were ingested by leukocytes, little or no killing of staphylococci could be detected. Subsequent studies indicated that certain staphylococci could survive for long periods within both human and rabbit polymorphonuclear leukocytes and that this ability correlated well with . . . pathogenicity. . . . Strains of coagulase-positive staphylococci isolated from human infection invariably survived for four to five hours within the interior of polymorphonuclear leukocytes. In contrast, coagulase negative strains isolated from the skin, air, or anterior nares were almost uniformly killed within leukocytes during this time period. A sharp differentiation could thus be made between these two . . . species of staphylococci. Subsequent studies by Tompsett showed that such pathogenic staphylococci could also survive within mononuclear phagocytes obtained from rabbits while nonpathogenic strains did not.—D. E. Rogers, Observations on the Nature of Staphylococcal Infections, *Bulletin of the New York Academy of Medicine,* January, 1959.

FATALITY AFTER INJECTION OF SCLEROSING AGENT TO PRECIPITATE FIBRO-OSSEOUS PROLIFERATION

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A 50-year-old woman with a long history of lumbar and sciatic pain had only temporary and incomplete relief after conventional treatment. An attempt was made by another physician to stabilize the joints concerned by injecting a sclerosing solution into the ligaments about the lumbosacral joint. There was immediate pain, paralysis, and incontinence. In the following months symptoms of basilar arachnoiditis and hydrocephalus appeared. The patient was referred to the authors for treatment. Ventriculostomy, decompressive craniotomy, and other measures for reducing intracranial pressure failed because of the extensive adhesions. The sites described for the injection of the sclerosing solution lie near several dangerous areas where a needle might enter the subarachnoid space. This technique for stabilizing intervertebral and paravertebral joints is extremely unsafe.

In 1956 a monograph was published which indicated that the cause of low back pain in many patients was relaxation of the ligaments about the joints of the spine and pelvis.[1] The treatment advocated was the intraligamentous injection of a proliferating solution of the sodium salt of a vegetable oil fatty acid to develop a maximum amount of fibrous tissue and bone, thereby affording joint stabilization. At the time of publication of the monograph, 4,000 injections of such a solution had been made "within the ligaments of a variety of articulations with no unfavorable incident or sequelae." Cures were reported for over 90% of the patients treated.

Although this form of therapy, namely, the injection of a fibro-osseous proliferating solution into the joints, has been without unfavorable incident in the hands of its author, the case reported here demonstrates one of the possible tragic complications of such therapy undertaken by another practitioner using this method.

Report of a Case

A 50-year-old woman had intermittent attacks of low back pain and sciatica bilaterally for 15 years. Her discomfort was not accentuated by coughing, sneezing, or straining at defecation. There had been several episodes of minor trauma to the spine, but there was no single major precipitating factor responsible for her symptoms.

She was able to bend forward, tilt toward either side, and bend backward readily. A straight leg raising test gave negative results on the right side to a 90-degree angle; the results appeared to be positive at a 30-degree angle on the left side. Dorsiflexion of the foot accentuated her pain. However, when her attention was diverted, the left thigh could be flexed on the abdomen and the leg extended completely without discomfort. At that time, dorsiflexion of the foot caused no sciatic pain. There were no sensory or reflex changes. Her spinal fluid protein level was 44 mg.%. The patient improved on two occasions on a regimen of pelvic traction, bed boards, bed rest, a back brace, and sedation; but later she developed intermittent recurrence of her symptoms.

In June, 1957, the patient had her case reports transferred to a physican in another community who was using the injection technique for creating fibro-osseous proliferation of the ligaments with presumed stabilization of the joints. After a diagnosis of unstable ligaments of the back had been made, the patient was placed in a prone position on the table, the site of the lumbosacral joint was identified, and the solution (stated to be zinc sulfate in 2.5% phenol solution) was injected in the midline into the ligaments about the lumbosacral joint. She developed immediate severe pain in the legs, was paralyzed from the waist downward, and had loss of bladder control. On attempting to arise from the table she fell to the floor. She was hospitalized for several days at two hospitals in that community. During this time she gradually regained almost complete use of her legs, although from the time of injection she continued to require an indwelling catheter for bladder function and cleansing enemas for bowel care. Eventually she was discharged to her home for convalescence.

In September, 1957, the patient was treated at St. Joseph Mercy Hospital in Ann Arbor for severe cystitis and nephritis. On Oct. 27, 1957, she was readmitted to the hospital complaining of nausea, vomiting, paresthesias over the buttocks and legs,

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perioral numbness, blurred vision, headaches, and generalized malaise. She had developed diplopia due to a right sixth nerve palsy. On examining the fundi, 2 D. of papilledema were found, with retinal hemorrhages and engorged retinal veins bilaterally. She had a mild peripheral facial paresis on the right, progressive weakness of the right leg, nuchal rigidity, and slurred speech. A diagnosis of basilar adhesive arachnoiditis was made.

On Nov. 1, 1957, ventriculograms demonstrated a widely dilated ventricular system. Unfortunately the anteroposterior and occipital views were unsatisfactory. The so-called Swedish views taken in the anteroposterior and posteroanterior position with a horizontal beam exhibited a marked degree of hydrocephalus (fig. 1). In the brow-down view not only was air seen in the occipital horns but some was seen in the cisterna magna (fig. 2). This suggested the presence of a communicating hydrocephalus. Because of the markedly increased intracranial pressure, a ventriculostomy on the left side was performed to gradually decompress the brain and adjust it to pressure changes. The ventricular fluid contained 704 red blood cells and 493 lymphocytes per high-power field. The fact that the patient continued to have moderate hypertension in spite of 24 hours of ventricular drainage was regarded as an ominous prognostic sign.

On Nov. 4, 1957, with the patient under intratracheal general anesthesia, exploration of the posterior fossa was performed. Immediately after the positioning of the patient on the operating table, marked hypotension developed which had to be combated by tilting her into the extreme Trendelenburg position and administering phenylephrine (Neo-Synephrine) hydrochloride intravenously. Her vital signs were permitted to stabilize for an hour. Inasmuch as the patient's condition had deteriorated in spite of ventriculostomy during the 48 hours prior to operation, it was believed that she would not improve further and that this would be the last chance afforded her for relief of blockage of the cerebrospinal fluid due to adhesions at the cisterna magna. Therefore, suboccipital craniotomy was performed. When the posterior fossa was exposed and the dura opened, a markedly adhesive arachnoiditis was found about the rim of the cisterna magna.

Indigo carmine was injected into the ventricular system at the site of the posterior parietal ventriculostomy on the left. The contrast medium readily appeared in the fourth ventricle but could not flow beyond the cistern because of marked adhesions. These were separated with difficulty. A small rubber catheter could be passed upward through the aqueduct into the third ventricle without difficulty. Several attempts were made to enter the subarachnoid space at the base of the brain, but the adhesive arachnoiditis prevented stripping of membrane from the cerebellar hemisphere or the region of the cerebellopontine angle. It was therefore considered advisable to close the wound, leaving the ventriculostomy tube in situ, and in a few days perform a shunting operation to overcome the hydrocephalus. At the close of the operation the patient's blood pressure had stabilized to some degree but only with the aid of a continuous intravenous phenylephrine drip.

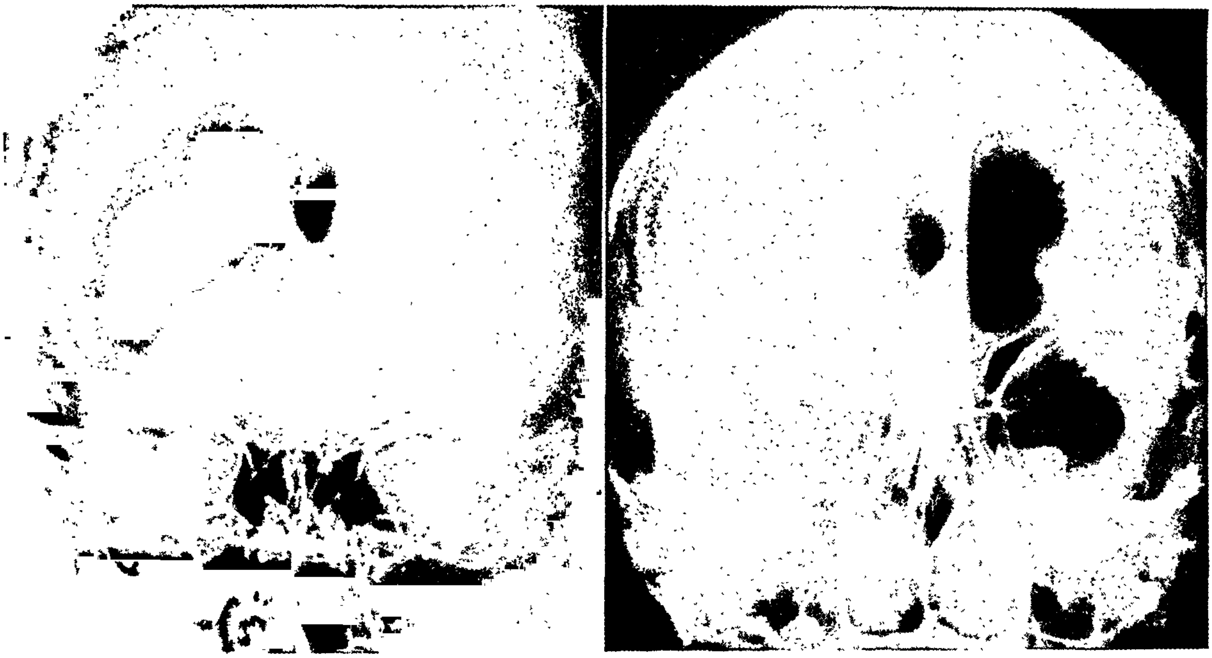

Fig. 1.—*Right*, anteroposterior and, *left*, posteroanterior ventriculographic views showing marked hydrocephalus.

Immediately after transfer of the patient from the operation table to the stretcher, it was observed that the pupils were dilated and had only a very faint reaction to light. This finding was thought to be due to cerebral anoxia secondary to the prolonged period of hypotension. It was believed that the adhesive arachnoiditis process had extended over the entire cerebrum and perhaps was responsible for widespread cerebral damage. In the recovery room the patient regained consciousness from anesthesia. Her reflexes were markedly obtunded and she was suffering from receptive and expressive aphasia. For the next six hours, vital signs were within a satisfactory range. However, at 7:30 p. m. her blood pressure abruptly rose to 220 mm. Hg systolic level and there were Cheyne-Stokes respirations. A large amount of cerebrospinal fluid had drained from the ventricular system through the ventriculostomy. In spite of the prompt administration of 100 cc. of 50% dextrose solution, the patient developed apnea and died suddenly at 8:10 p. m.

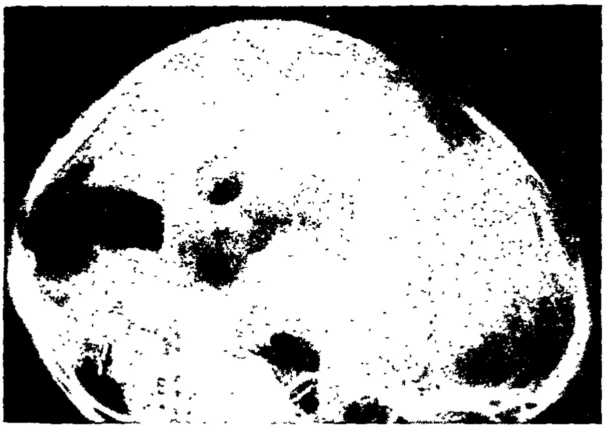

Fig. 2.—Brow-down ventriculographic view demonstrating dilated occipital horns and air in cisterna magna (*arrow*).

Postmortem Examination

At autopsy the entire spinal cord with the dura was removed by a posterior approach. There were some gross adhesions between the dura and inner meninges. An extradural hematoma found between the occipital bone and the dura measured 6 by 8 cm. and contained approximately 90 cc. of clotted blood. The inner meninges were not greatly thickened. The brain showed flattening of the convolutions and narrowing of the sulci due to cerebral edema. In the region of the parietal lobe the rubber catheter used in the ventriculostomy was demonstrated passing through the cerebral cortex into the left lateral ventricle, which was slightly dilated. The pons and medulla were symmetrical, with equivocal gross evidence of an adhesive arachnoiditis.

Microscopic Examination.—There was both an acute and chronic pattern observed in the study of this brain and spinal cord. Acute inflammatory changes were limited to the base of the brain in the posterior fossa and the upper cervical spinal cord.

Around the major vessels near the fourth ventricle there was perivascular infiltration. The choroid plexus was markedly infiltrated (fig. 3). The brain tissue exhibited some edema and generalized gliosis. In the lateral ventricles there was marked subependymal gliosis with astroglial proliferation and nodule formations in the ependymal layers. Granular ependymitis was demonstrated in the floor of the third and fourth ventricles.

The lower part of the spinal cord was markedly edematous and showed active gliosis with degeneration of numerous nerve fibers. The most marked chronic changes were demonstrated in the spinal cord. The dura and meninges had fused together and were frequently indistinguishable. The spinal meninges had compressed the cord and anterior and posterior spinal roots (fig. 4). No signs of acute inflammation were seen in the cauda equina. Here the connective tissue was dense, acellular, and partially hyalinized, with the most conspicuous feature being the marked connective tissue proliferation around the blood vessels, representing an old chronic periarteritis (fig. 5).

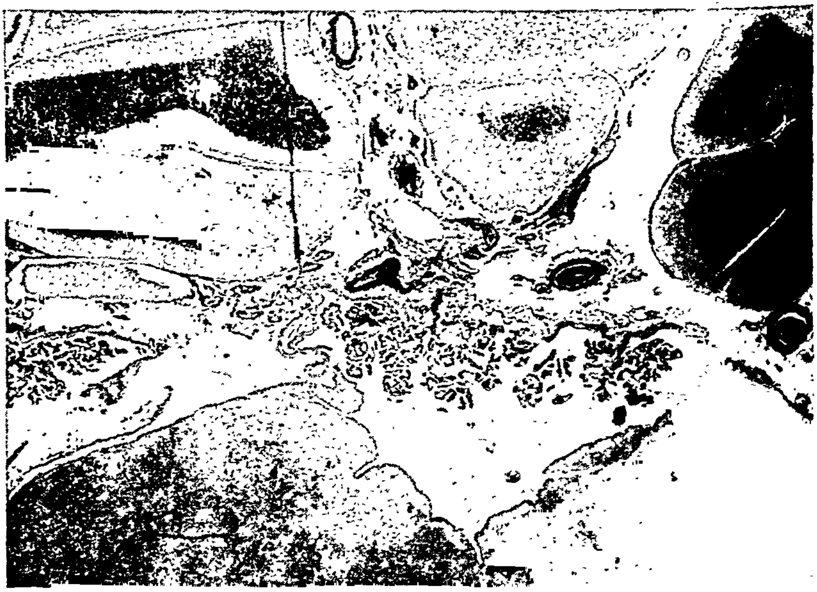

Fig. 3.—Area of fourth ventricle. Pronounced acute inflammatory changes (fibrin and cellular infiltration) of cerebellar meninges and choroid plexus.

The acute and chronic pathological pictures were independent of each other and could easily be separated, since the chronic scarification process was of an ascending nature and most pronounced around the lowest spinal cord segments. These findings definitely increased around the medulla, cerebellopontine angle, and the base of the brain. On the other hand the acute inflammatory changes, which were apparently secondary to the introduction of the ventriculostomy tube, the rubber catheter, and the indigo carmine contrast medium, were most marked in the posterior fossa and could be detected as isolated foci at the medullary and upper cervical levels. The continuous spread of the inflammation was apparently stopped by previous obliteration of the subarachnoid space.

Comment

The pathological specimens indicated diffuse involvement of the entire central nervous system. This patient was doomed at the very onset, regardless of the approach made to her problem. Although the sclerosing solution was injected accidentally into the subarachnoid space, the general pattern of the neurological complications followed rather closely those due to adhesive arachnoiditis secondary to some substances which have been deliberately introduced into the space for diagnostic, anesthetic, or therapeutic purposes.

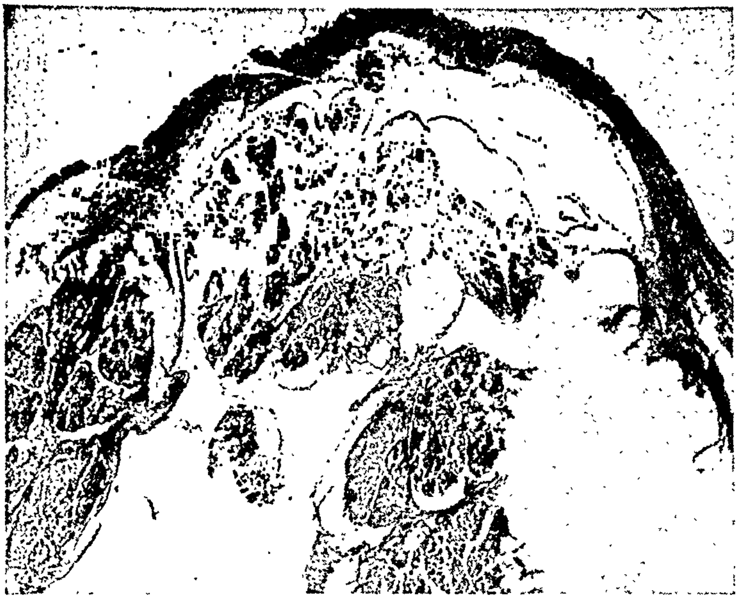

Fig. 5.—Cauda equina. Marked proliferation of perineural connective tissue.

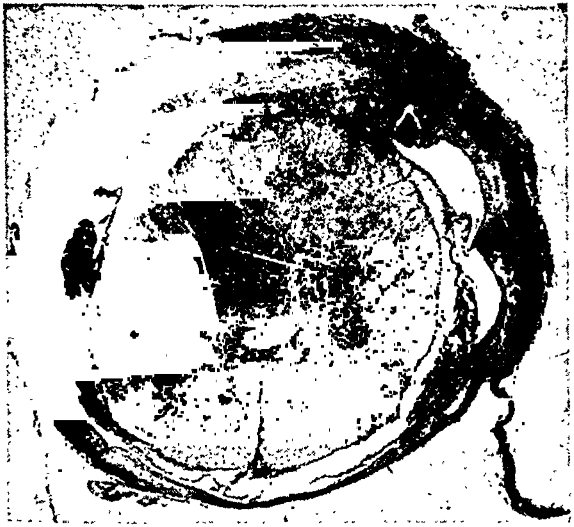

Fig. 4.—Spinal cord with dura and pia fused together. Note posterior root ganglions embedded in proliferated connective tissue.

Kennedy and others called attention to the grave complications involving the central nervous system, associated with spinal anesthesia, when they reported 3 cases [2] in 1945 and subsequently added 12 more case reports [3] in a comprehensive review of the topic in 1950. They indicated that the time interval between the actual injection of the anesthetic and the development of the lesion may be so great that the connection between cause and effect is not realized by the anesthetist or the surgeon.

Paddison and Alpers [4] presented a case of adhesive arachnoiditis occurring after spinal anesthesia, but they attributed this lesion not to the anesthetic agent but rather to the detergent cleaning material used. The entire neuraxis was involved in a progressive process with its onset 24 to 48 hours after the administration of the anesthetic agent and its termination in death 63 days later, a day after the patient had ventriculography for a marked internal hydrocephalus. The posterior fossa was not explored. A complete postmortem examination included a description of the pathological changes in the spinal cord and brain stem.

Erickson and Baaren [5] published a report of a 33-year-old man who for two days after myelography had a fever and a flushed face but recovered completely. For nine months he was asymptomatic, but then he developed neurological signs and symptoms due to an exudate adhesive arachnoiditis which produced obstruction of the fourth ventricle and basilar cisterns, leading to death 15 months after the myelogram had been taken.

The latter two cases are very similar to the one reported here in that there was a brief acute phase of disability and then a relatively silent period during which the adhesive arachnoiditis insidiously progressed. There was diffuse involvement of the entire neuraxis with complete involvement not only of the spinal cord but even of the brain stem, with sealing off of the ventricular system and internal hydrocephalus culminating in death.

A careful review of the sites described for the injection of the sclerosing solution to develop fibro-osseous proliferation[1] revealed that there are several very dangerous areas where a needle might penetrate the dura and enter the subarachnoid space. This might easily occur directly at the lumbosacral joint or laterally in the subarachnoid space of the cuff or sleeve of the nerve roots. In the prescribed technique it is stated that a solution of local anesthetic is injected just in advance of the sclerosing solution. This, of course, removes all pain and permits a painless injection.

In the instance reported here it must be emphasized that the sclerosing solution was not the usual sodium salt of the vegetable oil fatty acid as described in the original monograph but instead a solution of zinc sulfate in 2.5% phenol solution. However, it matters little what sclerosing solution was used, for it would effect its proliferative response in any type of tissue into which it was injected. The amount injected (reported as approximately 2 cc.) seems minute enough, but even when diluted by the complete cerebrospinal fluid content throughout the entire subarachnoid space it was sufficiently powerful to have its devastating effect on the whole neuraxis. Firm adherence to the arachnoid has a constricting effect not only on the neural tissue itself but also on the vascular supply to the brain and spinal cord.

In treating this patient, the neurosurgeons found themselves caught in the unenviable situation of trying to correct an impossible situation, i. e., to relieve increased intracranial pressure in a truly hopeless lesion. The extradural hematoma of the posterior fossa in this case must be listed as an operative complication and immediate cause of death. It no doubt was due to hemorrhage from a large vein which was not bleeding at the time of wound closure but which subsequently opened to fluctuations in the continuous artificially supported blood pressure by the administration of vasopressor agents.

Summary

A patient with low back pain and leg pain was accidentally injected with a sclerosing solution into the thecal canal. It is tragic that the solution entered the subarachnoid space and caused an extensive adhesive arachnoiditis of the entire brain and spinal cord with the development of a noncommunicating hydrocephalus. An attempt at surgical correction of this apparently hopeless situation resulted in death. This technique of precipitating fibro-osseous proliferation appears to be neither sound nor without extreme danger.

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FORMALDEHYDE IN WRINKLE-PROOF APPAREL.—Although it is rare, the following letter demonstrates that tears for milady may have an unemotional source. "There is some sort of gas—or condition—in the dress store I manage that causes our employees to have burning, stinging eyes and headaches. Customers coming into the store are also affected." . . . Many possible sources were investigated; ammonia leaks from refrigerators, freon gas escaping from air conditioners, gaseous products of combustion given off by heating appliances and even sewer gas. Not guilty! . . . The Ohio Department of Health had an inkling of the trouble—formaldehyde gas. . . . Health agencies in New York and Baltimore had reported similar complaints from cloth finishing mills and dress shops. Moreover, the physical symptoms and reactions of the people working in the dress shops matched the recorded symptoms caused by exposure to formaldehyde gas. . . . The air, in several dress shops from which complaints had been received, was tested for formaldehyde gas. Sure enough, the air did contain from 0.13 to 0.45 parts of formaldehyde per million parts of air. Not enough to cause illness, but sufficient to be intensely irritating.—H. B. Bourne Jr. and S. Seferian, Formaldehyde in Wrinkle-proof Apparel Produces Tears for Milady, *Industrial Medicine and Surgery,* May, 1959.

RESPONSE OF TRIGEMINAL NEURALGIA TO "DECOMPRESSION" OF SENSORY ROOT

DISCUSSION OF CAUSE OF TRIGEMINAL NEURALGIA

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Two series of patients with tic douloureux were followed up after surgery. In one series of 100 patients (Cleveland series) the extradural approach was used and the sensory root of the trigeminus was freed from its dural sleeve and otherwise manipulated; in the other (Copenhagen) series of 100 patients the approach was intradural, was less apt to traumatize the semilunar ganglion, and caused less postoperative sensory impairment. In the combined series, 62% of the patients reported complete relief, 11.5% had mild recurrences, and 26.5% had severe recurrences. Some degree of sensory loss was present in 26% with successful treatment and in 28.3% of those in whom the treatment failed. Neither surgical trauma to the nerve root nor incision of its dural sleeve were essential to the success of the operation. The critical part of the operation appeared to be a neurolysis or manipulation of the sensory root at the point where it crosses the apex of the pars petrosa of the temporal bone.

Decompression of the sensory root was performed on 112 patients with trigeminal neuralgia (tic douloureux) between January, 1953, and March, 1955. Two of these patients died in the hospital and 10 were lost to follow-up within one year. The remaining 100 patients, with the exception of 5 who died in the interval, were followed for three and one-fourth to five and one-half years and constitute the basis of this analysis.

Results of Decompression Operation

Sixty-seven patients had no paroxysm of tic douloureux after recovery from anesthesia of the operation. Of the remaining 33, 8 have had only mild recurrences and are happy with the result. For 25 patients the initial operation failed to afford satisfactory or lasting relief. Two of these patients, because of continuing pain while still in the hospital, required a revision of the operation. The revision, consisting of reexposure and further manipulation of the nerve root, was followed by lasting relief in one patient and by mild recurrence after three and one-half years in the other; however, because a second procedure was required these two cases have been classified with the failures. Twenty-three patients experienced severe recurrences after a postoperative period of relief, and 19 of them had subsequent operative procedures. Six of these had a second decompression, followed in four instances by a second recurrence. (One of these latter patients has severe multiple sclerosis with bilateral trigeminal neuralgia and refused to have the second nerve cut. Dividing the great auricular nerve, after the method of Wyburn-Mason,[1] was without effect.) Ten had resection of the sensory root, one alcohol injection, and two exploration of the nerve in the posterior fossa. In one of the latter patients, an anomalous arterial loop was found lying against the nerve; the pain was completely relieved after separating this vessel from the nerve root by the interposition of a piece of absorbable gelatin sponge (Gelfoam). In the second patient the pain was relieved after the removal of a large meningioma attached to the lateral sinus on the side of the pain. Of 33 patients with recurrence or persistence of pain, therefore, 21 have had reoperation and 12 have not. In eight of the latter the recurrence thus far has been so mild that reoperation has not been indicated.

Of the 67 patients who had complete and lasting relief after decompression, 7 exhibited sensory loss before operation because of previous treatment. Of the remaining 60, 23 (38%) had postoperative subjective numbness or demonstrable sensory loss or both. Of the 33 patients who had a mild or a severe recurrence, 3 exhibited sensory loss from previous treatment. Of the remaining 30, 13 (43%) had postoperative subjective numbness, demonstrable sensory loss, or both. These comparative percentages indicate that impairment of sensation resulting from trauma of the operation was not a factor contributing to the success or failure of the operation.

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Operative Methods

These patients were operated on by one surgeon (W. J. G.) using the extradural approach of Frazier with the patient in the sitting position. After the dura had been opened anterior to the petrous ridge, the dural sheath over the sensory root was incised back through the petrosal sinus into the tentorium for a distance of 1 cm. posterior to the apex of the petrous portion of the temporal bone. The sensory root was freed from its dural sleeve, gently brushed with a cotton pledget, and irrigated with Ringer's solution.

Taarnhøj, using his intradural approach with the patient in the horizontal position, followed 100 patients in his Copenhagen series for three to six years.[2] Fifty-seven of these patients had no recurrence of tic pain, while in 15 the recurrence was so mild that the operation could be considered successful. In 28 cases, the operation failed to afford satisfactory or lasting relief. Nine of these patients had a second decompression, nine had resection of the sensory root, and eight had alcohol injection; two did not have reoperation.

Fewer patients in the Copenhagen series than in the Cleveland series exhibited postoperative sensory impairment. It was present in 14% of those with a good result and in 11.6% of those in whom the treatment failed. The lower incidence of sensory loss in the Copenhagen series probably is due to the fact that the intradural approach is less apt to result in trauma to the ganglion.

Considering the Cleveland and the Copenhagen series together, 62% had complete relief, 11.5% had mild recurrences, and 26.5% had severe recurrences. Some degree of sensory loss was present in 26% with successful treatment and in 28.3% of those in whom the treatment failed. These figures indicate that sensory loss is not essential to success and, therefore, that the relief of pain is not the result of interruption of nerve impulses. That trigeminal neuralgia can be immediately relieved by an atraumatic manipulation of the nerve root suggests that the cause of this pain, whatever it may be, is located in this portion of the trigeminal system.[3]

Other intracranial operations on the trigeminal system that do not sever the nerve have afforded relief from trigeminal neuralgia. Sheldon and associates[4] described relief by an intracranial "decompression" of the second and third divisions of the nerve; they accomplished this by enlarging the foramens of exit with a dental drill. They subsequently discovered that trigeminal neuralgia could be relieved more effectively by "compression" of the posterior root than by decompression of its peripheral branches and that incision of the dural sheath was not essential to success. Therefore, they concluded, the relief of pain in these cases was due to surgical trauma to the nerve rather than to relief of pressure as Taarnhøj had hypothesized. Stender[5] relieved trigeminal neuralgia by opening the cavum mecklii, an operation which he described as "gangliolysis." However, regardless of the terms applied to them, the common feature of these intracranial procedures is manipulation of the sensory root. Even the retraction of the dura incident to introducing a dental drill into the foramen rotundum or ovale is bound to exert some indirect traction on this structure.

That the relief is due to manipulation (neurolysis) of the sensory root and not to compression or decompression of the root, the ganglion, or the peripheral branches is indicated by an experience which Taarnhøj[6] described as follows: "In some patients with trigeminal neuralgia in this series, suspected to have tumors in the cerebellopontine angle, a cerebellar approach was performed, but no tumor was found. . . . A hook then was put into the porus trigemini—i. e. the opening where the root leaves the cavum Mecklii—and an attempt was made to enlarge the porus a little in different directions in order to free the root from possible adhesions. Although no real decompression was performed in the 5 patients treated in this way, they were all free from pain after the operation, and the sensibility was normal." This author, therefore, has shown that, via either a middle or a posterior fossa approach, trigeminal neuralgia may be relieved by a manipulation of the sensory root carried out so gently that no sensory loss results.

In 627 operations for trigeminal neuralgia via the middle fossa, Ruge and co-workers[7] found six meningiomas of the dural envelope of the gasserian ganglion. In 473 operations via the posterior fossa at the Johns Hopkins Hospital,[8] 24 tumors were encountered. These two series indicate that trigeminal neuralgia is associated with a tumor located in the middle fossa (1%) or in the posterior fossa (5%). Inasmuch as the posterior root constitutes the only part of the trigeminal system common to both fossae, this again suggests that the cause of the pain is located in the posterior root.

Comment

The tendency to consider trigeminal neuralgia a disease rather than a symptom has obscured thinking on the subject. Harris,[9] for instance, found it to be a "complication" of multiple sclerosis in 64 of 1,622 cases; in one such case studied at autopsy, Parker[10] demonstrated a sclerotic plaque on the sensory root.

Where tumors, anomalous blood vessels, or other obvious lesions involving the nerve are not present in cases of trigeminal neuralgia, there still remains the anatomic fact, pointed out by Lee,[11] that in man the sensory root of the nerve is angulated at the point where it crosses the apex of the petrous bone. In a roentgenographic study of the skulls of 130 patients with trigeminal neuralgia, Gardner and co-workers [12] measured the relative heights of the apexes of the petrous bones at this point. In 60% of the patients the apex of the petrous bone on the neuralgic side projected higher into the cranial cavity than it did on the opposite side, while in only 20% was this relationship reversed. Their studies also showed that a progressive upward migration of the dens occurs between the fourth and eighth decades in women with trigeminal neuralgia. This progressing basilar impression, they believed, was due to postmenopausal osteoporosis. In these cases the apex of the right petrous bone was usually pushed higher into the cranial cavity than the left, and this was advanced as a possible explanation for the fact that trigeminal neuralgia is more commonly encountered on the right side and in elderly women. These authors pointed out that trigeminal neuralgia also may be a symptom of basilar impression of the congenital variety or of the acquired form that accompanies Paget's disease of the skull.

In view of the evidence cited above we believe that the cause of trigeminal neuralgia may be localized to the posterior root of the fifth cranial nerve with almost as much certainty as the cause of brachialgia and sciatica may be localized to the posterior root of a spinal nerve. In this connection it is interesting to note that Frykholm,[13] also a Scandinavian, relieved brachialgia by incising the dural sheath of the angulated sensory root of the spinal nerve just as Taarnhøj, some years later, relieved trigeminal neuralgia by incising the dural sheath of the angulated sensory root of the trigeminal nerve.

Because trigeminal neuralgia can be relieved by alcohol injection of a peripheral branch of the nerve, Rowbotham [14] and others have suggested that the cause is peripheral to the ganglion. This theory is countered by the fact that, even though trigeminal neuralgia associated with a tumor in the posterior fossa can be relieved temporarily by a peripheral alcohol injection, it can be permanently relieved by a removal of the tumor carried out so carefully that it produces no sensory loss.[15]

In 1937, Frazier and associates [16] suggested that the lesion responsible for trigeminal neuralgia lies in the thalamic-cortical connections. Recently, King and co-workers [17] advanced experimental evidence that suggests that the cause of trigeminal neuralgia could be in the descending nucleus of the trigeminal nerve. These theories, however, fail to explain why trigeminal neuralgia may constitute a symptom of a tumor compressing the nerve root and why the "idiopathic" variety can be immediately relieved by manipulation of the root where it crosses the apex of the petrous bone. Even the evidence advanced by Wyburn-Mason [1] that this pain may be relieved in some cases by resecting the great auricular nerve does not render the root theory of origin invalid. It indicates that the trigger mechanism in some patients is supplied, in part, by fibers of the cervical plexus that overlap the distribution of the trigeminal nerve.

In view of Dandy's [18] demonstration of the frequency with which the posterior fossa approach will disclose a cause for trigeminal neuralgia, it is not surprising that the middle fossa approach of Taarnhøj frequently fails to afford lasting relief. Therefore, it is now our custom to search for a lesion in the posterior fossa in those patients who develop a recurrence of trigeminal neuralgia after a neurolysis of the sensory root in the middle fossa. If the approach via the posterior fossa does not disclose a lesion, the nerve root is gently manipulated with a nerve hook introduced into the dural foramen, as practiced by Taarnhøj.[6] The results of this method of dealing with recurrences will be reported when an adequate follow-up sample is available.

Summary

A three-to-six-year follow-up study of 200 patients in whom "decompression" of the sensory root was done for trigeminal neuralgia (tic douloureux) revealed that 62% had complete relief, 11.5% had partial relief, and in 26.5% the operation failed. Neither surgical trauma to the nerve root nor incision of its dural sleeve is essential to its success. The critical part of the operation appears to be a neurolysis or manipulation of the sensory root at the point where it crosses the apex of the petrous bone.

Trigeminal neuralgia is a symptom—not a disease. It may constitute a symptom of multiple sclerosis, of basilar impression, or of a tumor located either in the middle or in the posterior fossa. "Idiopathic" trigeminal neuralgia may be relieved by a gentle manipulation of the sensory root via either a middle or a posterior fossa approach. The only portion of the trigeminal sensory system that is common to both the middle and the posterior cranial fossae is the sensory root. The cause of trigeminal neuralgia, therefore, presumably lies in the sensory root.

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CANCEROPHOBIA AND DELUSION

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There are two types of patients who consult physicians in connection with the fear of having cancer and in whom malignancy cannot be detected. Those who fall into the cancerophobia classification can accept reassurance and regain normal status. Those who present the delusion of cancer are unable to accept reassurance and become increasingly anxious. In this second group, need for psychiatric treatment may be overlooked even when it has become urgent. It is important to differentiate between the two groups.

The general practitioner will fairly often be consulted by a middle-aged patient with a history of vague pains and aches more or less well localized and of fairly recent onset who on physical examination will not yield any findings of organic illness which would explain the symptoms. It might be only after repeated visits that the patient will confide and mention to the physician his fear of having cancer. Once this fear is voiced and discussed, most patients will be able to accept reassurance as to the absence of such illness and the symptoms will disappear with the medication prescribed, usually a mild sedative or analgesic.

By and large the physician does not discourage his patients from seeking consultation on such an "imaginary" ailment, mainly because he recognizes the tremendous importance of early detection of cancer. On the contrary, most physicians will encourage their patients to seek them out whenever they feel that something might be seriously wrong with their bodies. At the same time, the physician also expects his patient to be able to accept his considered opinion that nothing is seriously wrong and that there is no evidence of cancer. Most patients can do that, but some cannot.

As far as the patient is concerned who comes to the general practitioner with "cancerophobia" and is able to accept reassurance as to the absence of cancer, the following psychodynamic considerations seem to apply: For some extraneous reason not connected with his physical health, the patient experiences a sudden rise in anxiety and feels threatened and insecure. As a result he becomes overly concerned with his body and body functions. Some vague pain or sensation which under ordinary circumstances would probably have been disregarded altogether now becomes the focus of anxiety and increased tensions which in turn set up a vicious circle by increasing the sensitivity and perceptiveness in that area. Once this circle of anxiety/organic symptoms is set in motion and as the pain and dis-

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comfort loom bigger and bigger in the mind of the patient, the fear of the unknown replaces or overshadows completely the original anxieties. This fear is expressed in whatever socially or culturally acceptable form of physical illness is prevalent at the time, currently, the fear of cancer. (Not so long ago it was the fear of tuberculosis.) In consulting his physician, the patient can get reassurance and regain his old feeling of security without the original anxieties ever coming to the surface.

There are other patients who will often present themselves initially with very similar complaints to those described but will be unable to accept reassurance. Such a patient's symptoms do not respond to such medication as mild sedatives, analgesics, or "tranquilizers." He will return repeatedly with the same complaint and show increasing anxiety and desperation over the physician's inability to help him. And, as his complaints intensify, it will finally be apparent that his fear, his belief that he must have cancer, is very deeply seated indeed and not accessible to correction by such measures as reassurance. At this point it becomes extremely important to recognize that the simple diagnosis of cancerophobia is no longer applicable. To be described in these terms, the fear of cancer has to be recognized by the patient as being irrational and it has to be accessible to correction by a new experience, namely, physical examination and perhaps some of the usual laboratory tests, followed by reassurance that all is well. If the fear persists, it merits the designation of "delusion," a fixed idea which corresponds in its emotional direction to the affect of the patient and which is not accessible to correction as long as the emotional condition persists which really gave rise to it in the first place.[1]

The differentiation between cancerophobia and the delusion about having cancer is not merely a semantic exercise but has great practical importance. The delusion usually is a symptom of a very serious underlying condition. If the physician does not recognize it, he will probably lose his patient, either to another physician or because of suicide.[2] But once he is alerted to the importance of the presenting symptom and its implications, the physician will easily discover a number of other symptoms which the patient has either not mentioned at all or which he has presented simply as difficulties resulting from the chief complaint, his fear of having cancer. He will probably find the patient suffering from insomnia with early morning waking, loss of interest in his usual pursuits and in his environment, loss of appetite with some recent weight loss, disturbance of concentration, and increased emotional lability with depressive affect. The general practitioner might get this history from a new patient who is consulting him after leaving his former family physician who "couldn't give me satisfaction, didn't help my condition." Statements such as these, on closer inquiry, will be found to mean that his physician could not find any organic illness which would explain the patient's concern and anxieties. Sooner or later such a patient might be hospitalized for further studies, usually with the same negative result as to finding of "organic" illness.

In these cases the correct diagnosis is usually one of a severe depressive reaction, especially if the patient is in the age group 45 or over. In younger patients a similar clinical picture will usually be presented in more bizarre language and be less fixed to any one organ, moving from one organ system to another; the possibility of a schizophrenic reaction should then certainly be seriously considered.[3] At any rate, the presence of a delusion of having cancer merits serious attention by the physician, and a psychiatric consultation is usually indicated.

Report of Cases

Case 1.—A 60-year-old married man was referred to the hospital with the chief complaint of backache. The backache was of fairly long standing but had become rapidly worse during the previous months to the point where the patient had to interrupt work about two months prior to admission. He had consulted an osteopath, a chiropractor, and several physicians. He had been hospitalized twice in the local hospital, many x-rays had been taken, and different prescriptions had been given—all to no avail. The backache persisted and he was unable to return to his work. The diagnosis so far had been given as moderate arthritis of the spine and mild generalized arteriosclerosis.

When I saw the patient first, he was agitated, restless, and depressed and expressed his conviction that he must have cancer of the spine. Some suicidal preoccupations could be elicited. Diagnostically, he presented the clinical picture of an agitated depressive reaction, but there was also evidence of a clearly defined though not very gross brain deficit, although the patient himself at first denied any impairment of memory. The key problem was soon clarified as being that this man experienced with advancing age some deterioration of his mental capacities of which he was aware but which he denied. In addition there was increased demand and pressure at work resulting from certain changes in his employment. The combination of these two factors, namely, the mild organic brain syndrome associated with general arteriosclerosis on the one hand and the increased demands in his work situation on the other hand, really placed the patient in a "situation without issue." His reaction was a feeling of helplessness and hopelessness leading to an increasing withdrawal from social contacts and a rising preoccupation with body functions and body feeling, resulting finally in a progressive exaggeration of the mild back pain which had been present but not disturbing him much over the last few years. He developed the conviction that he must have cancer of the spine, and no amount of reassurance given could shake this conviction. His depressive mood, his agitation, his insomnia, and his loss of weight were all very plainly there to be seen and evaluated yet were not understood in their proper meaning because they were simply thought to be the "natural" reaction of a man who fears that he has cancer.

At the time of this patient's transfer to the psychiatric ward of a general hospital the depressive reaction had achieved such magnitude that he was no longer accessible to a psychotherapeutic approach and he was given a course of electroconvulsive treatments. He responded very well, and with the lifting of the depressive mood the back pain and the cancerophobia also disappeared. The task remained to help this man with further planning, to help him to a change of jobs which would permit him to exercise old overlearned skills which had not been affected by the slowly beginning mental (arteriosclerotic) deterioration and which would afford him gratification from areas of competence so that he could reestablish his self-concept at a comfortable level.

Case 2.—A housewife, aged 54, was admitted to the medical service of the hospital with the chief complaint of abdominal pain. The description of the pain was extremely vague and of changing location. She also complained about yellow stools and yellow urine, and there had been a 16-lb. (7.3-kg.) weight loss during the year prior to admission, apparently the result of marked anorexia. The patient had been seen by a number of doctors and had undergone a hemorrhoidectomy about six months prior to admission. Since then she had repeatedly voiced her conviction that she was suffering from cancer, which she thought was evident from the color and shape of her feces, from her weight loss, and from a general feeling that her muscles were just wasting away. No amount of medical attention could shake these beliefs; she changed physicians repeatedly in an attempt to gain help, but at the time of her admission to the psychiatric service she had reached the point where she felt that physicians could not be trusted any longer. She thought that there was a conspiracy of silence between them not to tell her the truth, namely, that she was suffering from cancer of the colon. Repeated physical examination and complete laboratory and x-ray studies had consistently shown her to be in good physical condition.

Psychiatric interviews revealed that the patient's preoccupation with her bowel function followed the death of her brother, who died from cancer of the colon. She soon thought she too had similar symptoms, and this led her to seek medical advice. Her complaints first led to a hemorrhoidectomy, but a short time after her discharge from the hospital she experienced the death of her mother, which further contributed to her depressive reaction. Unfortunately her emotional condition was not recognized by her physicians, who continued to treat her for the presenting symptom, abdominal pain. The referring physician mentioned that the patient had developed cancerophobia after the hemorrhoidectomy, yet he continued to treat her medically for her abdominal complaints, offering reassurance as to the absence of malignancy. Characteristically this referral to the hospital was made to the medical service, and psychiatric consultation was not requested at any time.

When I saw the patient first there could be no doubt about the presence of a depressive reaction which had reached psychotic magnitude. She responded well to a course of electroconvulsive treatments and has remained well for a two-year follow-up period.

Summary

The fear of having cancer is a fairly frequent phenomenon that brings patients to consult their doctor. There are two types of patients who present this symptom without having cancer: those who can accept reassurance that all is well and those who cannot and become increasingly anxious. This reflects a difference between cancerophobia and the delusion of having cancer. The latter is interpreted as a symptom of an underlying severe emotional disturbance which merits psychiatric consultation.

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FINGERTIP HYPERESTHESIA

SOLITARY SIGN OF NEW OCCUPATIONAL DERMATOSIS DUE TO SILICA HAIR CURLERS

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and
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Microfragments of silica embedded in the outer layers of the skin were detected by dark-field microscopy of superficial skin biopsies. Transfer from silicon hair curlers handled in the patient's occupation as a hairdresser was facilitated by the fact that daily contacts with alkaline hair sets and waving solutions served to soften the stratum corneum and epidermis. Precise and exactly localizable micropoints of hyperesthesia were identified. Cure was provided by a superficial razor shave biopsy. Prophylaxis must center on avoidance of the new silica rollers.

We wish to report a distinctive new entity seen as an occupational disease in a hairdresser. The solitary clinical finding was persistent punctate hyperesthesia of the fingertips. After considerable diagnostic study the hyperesthesia was demonstrated to be due to tiny particles of silica which became embedded in the epidermis, impinging on the sensory nerve endings. The recent widespread use of silica or sand-coated hair curlers suggests that such an *invisible foreign-body hyperesthesia* may become common among beauticians unless efforts are taken to eliminate this new occupational hazard. Furthermore, failure to recognize the entity may subject patients to extensive medical investigations which otherwise could be eliminated once the occupational nature of the problem is recognized.

Report of a Case

The patient, referred to us by Dr. Meyer Naide, was a 40-year-old woman in good health who first noted a marked sensitivity of the fingertips to light touch. This began in September, 1958, on the lateral side of the tip of the right fourth finger. Shortly thereafter the medial tips of both thumbs were similarly affected. Eventually all of the fingertips became involved to a greater or lesser degree. Pain and inflammatory changes were absent, but exquisite tenderness to touch continued. No other sensory changes had been noted by the patient.

She gave a history of a hysterectomy, an appendectomy, and the surgical removal of a sebaceous cyst, as well as the surgical repair of a rectal fissure. She denied any personal or familial history of diabetes mellitus, skin disease, neurological disease, or Raynaud's disease. She did claim to be "allergic" to penicillin. For many years she had been employed as a hairdresser, and she gave no history of new contactants at work or home. Born in Texas, she had lived in Philadelphia for the past 16 years. She stated that she did not drink alcoholic beverages but that she did smoke a pack of cigarettes a day.

Prior to our studies she had been seen by a number of physicians who had considered a variety of presumptive diagnoses, including glomangioma (glomus tumor), peripheral neuritis, peripheral vascular disease, erythredema polyneuropathy (acrodynia), cervical rib syndrome, hysteria, spinal cord lesion, malingering, syringomyelia, and tumor.

During a hospitalization the following studies and results were reported: hemoglobin level 15.1 Gm.%; white blood cell count 7,800 per cubic millimeter, with 74% neutrophils, 23% lymphocytes, 2% monocytes, and 1% eosinophils; hematocrit value 48%; urinalysis, occasional hyaline and finely granular casts and 4+ protein; serum Kolmer and Kline tests, nonreactive; blood urea nitrogen level 10 mg.%; sugar level 83 mg.%; calcium level 9.1 mg.%; phosphorus level 2.7 mg.%; protein level 5.8 Gm.%, with albumin 3.3 and globulin 2.5; and x-rays of chest, hands, and cervical spine normal.

General physical examination was noncontributory. Neurological consultation revealed no objective evidence of disease. Results of vascular studies were likewise normal. The fingers were warm and had equal surface temperatures. Radial and ulnar pulses were normal, as were oscillometric readings. Studies on her reactive hyperemia and also vasodilatation tests disclosed a normal circulation in the fingers. Treatment with a variety of local anesthetic and steroid creams was unavailing. Likewise, a short course of systemic prednisolone (Meticortelone) therapy was reported to be without effect.

We first saw the patient in consultation at the end of November, 1958. At that time she was unable to work because of the incapacitating hyperesthesia of the fingertips. Gross examination revealed normal skin. Sweating patterns on the hands were also entirely normal. However, under Zeiss stereoscopic surface microscopy (80 ×), fine fissures could be seen in the stratum corneum of the thumbtips. Microsensory testing revealed these to reflect the exact areas of tenderness.

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Specifically questioning the patient regarding abrasive materials, we were then able to elicit the fact that three months prior, coincident with the appearance of her fingertip problem, she had first begun to use a new "silicon hair curler." She described handling as many as 450 of these a day, six days a week, for nearly three months. These silicon hair curlers were covered with a fine granular material, presumably sand glued to a cardboard roller. In the course of use, the curlers lost their rough surface and, once smooth, had to be discarded. Prior to the exclusive use of these new curlers the patient had been using regular rubber and plastic curlers. In addition to the contact with the silicon curlers, the patient had considerable daily "wet work" with alkaline hair sets and waving solutions. It became apparent that tiny invisible fragments of the silica material from the curlers might have become embedded in the softened macerated stratum corneum and epidermis as a result of constant use of the curlers.

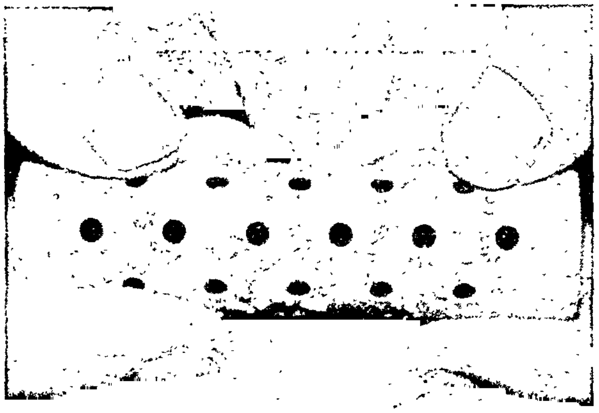

Fig. 1.—View of silica hair curler, showing surface rough with irregularly glued grains of silica. As curler is twirled, points of maximal friction are at medial tips of thumbs and tips of fourth fingers.

Many observations and tests confirmed this. First, the gross hyperesthetic areas proved to be exact points (fig. 1) of maximal friction between skin and curler.

Second, the curler particles, measuring 0.5-1.0 mm., were found to fragment easily into microparticles (5-100μ). Spectroscopic examination revealed them to be essentially silica. Silicon was the major component, with less than 0.1% each of aluminum, iron, calcium, magnesium, titanium, and copper present. The following elements were checked, but not found: chromium, boron, cobalt, cadmium, lead, columbium, manganese, gallium, nickel, germanium, silver, gold, sodium, molybdenum, zinc, platinum, antimony, strontium, arsenic, tellurium, barium, tungsten, beryllium, vanadium, bismuth, and zirconium.

Third, the hyperesthesia could be shown to be composed of many micropoints of hypersensitivity. Such study was done with use of a micropoint (30μ) stimulus. The points of pain on pressure were precise and exactly localizable. All of the discernible microfissures were hypersensitive, but many hypersensitive points could be found where the overlying skin was entirely normal at 80 ×. All of the testing was done under high-power stereoscopic visualization with a micropoint stimulator and in such a way that the patient was unaware of the point of stimulus. Significantly, the points remained constant in site and attempts to secure varying sensory responses from the patient met with failure. The exact number of hypersensitive points was high. For example, careful mapping of the right fourth fingertip revealed 22 distinct puncta. The points were remarkably discrete, so that testing the skin from 100μ away gave a negative report. Finally, the hyperesthesia was always appreciably less when the stratum corneum was dry.

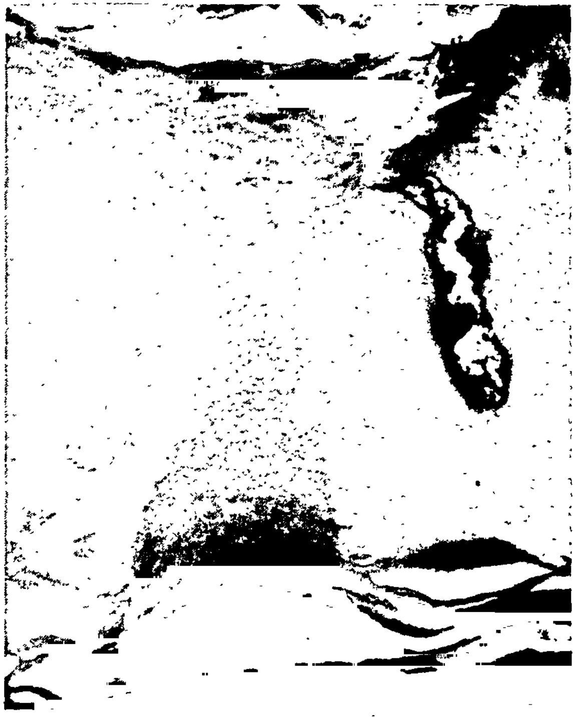

Fig. 2.—View of epidermal biopsy from tip of patient's finger, showing site of entrance of irregular particles of sand from hair curler. Part of foreign material has fallen out during sectioning, but shape of gross particle can be seen as lacuna in stratum corneum (210 ×).

Fourth, superficial skin biopsies were obtained (December, 1958) and study of complete serial sections revealed many black foreign bodies in the stratum corneum (fig. 2) and a lesser number in the lower epidermis. An occasional particle was seen in the upper papillary layer of the dermis. In some specimens ragged lacunae could be seen which were presumed to be the site of the silica prior to sectioning. It was possible to see the points of entry of some of the larger particles. Some pressed directly on the Meissner tactile corpuscle of the dermal papilla (fig. 3). Significantly, some of the histological particles could easily be dismissed as "dirt on the slide or stain precipitate" by the casual examiner. Only by being alert to the possible appearance of these grains and by using serial sections was it possible to track down the offending mechanical agent. Conclusive evidence of the identity of the intraepidermal particles and the silica of the rollers was provided by darkfield microscopy. Under this form of lighting the particles no longer were dark but became refractile with minute concentric ring formations seen under photography in both the tissue foreign material and the silica fragments.

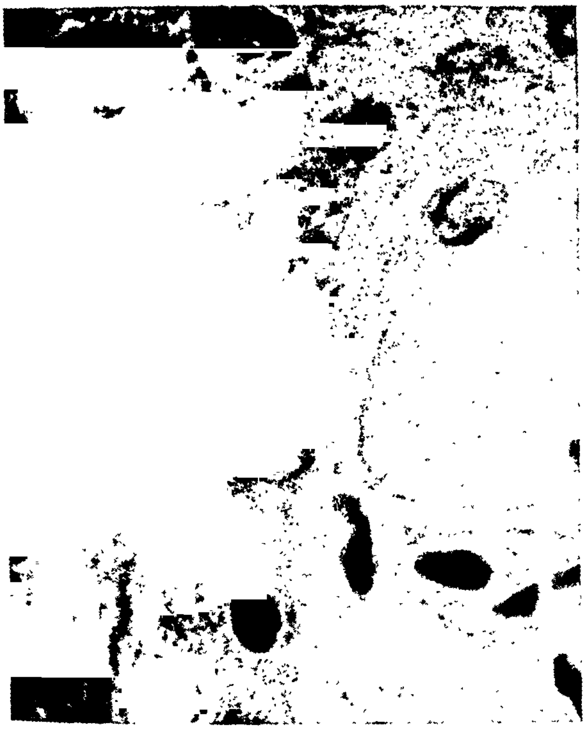

Fig. 3.—View of irregular black silica particle in epidermal rete peg, impinging on Meissner's corpuscle in dermal papilla (right). Nerves are not stained, but typical collagen whorl of Meissner's corpuscle can be seen (1,360 ×).

Once the cause had been detected, it was possible to offer a cure. The superficial location of the material has made it possible to remove the cause of the hyperesthesia by a superficial razor shave biopsy.[1] This requires no sutures and heals well. In this patient the operation was followed by temporary numbness and hyperesthesia. In all, the operation was performed on five of the fingertips.

Comment

We have described a new occupational hazard for hairdressers, which to our knowledge has not been previously reported.[2] Clinically occult, the problem presents itself as a punctate, highly localizable hyperesthesia of the fingertips. In some instances under high magnification the skin surface may reveal tiny fissures, but in others the skin may be entirely normal. It thus becomes an "invisible occupational dermatosis" readily recognized only after securing the history of contact with silica hair curlers. Skin biopsy will confirm the diagnosis of revealing microscopic intraepidermal silica particles at the points of fingertip tenderness. It can be seen that the silica fragments will penetrate the macerated skin of persons who have their hands in various rinses, sets, and wave solutions. Furthermore, the degree of exposure will in part be a determinant. *We have no knowledge of the factor of individual* susceptibility. Differential diagnosis will include neurological or peripheral-vascular disorders. Indeed, the patient may never have been seen by a dermatologist because of the absence of objective cutaneous signs. Glomangioma remains the condition which will most likely simulate this entity.

Prophylaxis must center on the avoidance of these new silica rollers. The degree of hazard cannot be accurately assessed at present, but it appears probable that repeated daily contacts with the silica roller might produce symptoms in a high proportion of professional beauticians and make avoidance of the device mandatory.

Active treatment consists in removal of the foreign material. Generally, it would appear this can best be done by a superficial razor shaving of the top layer of skin. Local as well as systemic medical treatment would seem to be ineffective. However, if the particles are all intraepidermal, it might be anticipated that over a period of months spon*taneous shedding and cure could occur.*

Summary

A new, invisible occupational dermatosis, clinically mimicking glomangioma, occurred in a hairdresser. It consisted of punctate hypersensitivity of the fingertips resulting from entrance of foreign particles of silica. These silica particles rubbed off a new type of hair curler and became embedded in the macerated outer layer of skin. Microsurgical treatment was successful in the case reported.

University Hospital, 36th and Spruce streets (4) (Dr. Shelley).

Mr. Edward F. Glifort did the photographic work in this study.

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AUTOMATIC DETECTION AND RECORDING OF CARDIAC ARRHYTHMIAS

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The cardiac monitor here described is a portable instrument used in connection with a standard electrocardiograph. From this source the monitor receives impulses which are amplified and interpreted, actuate the recording mechanism, cause an alarm to sound, and can, optionally, start up an electrical cardiac stimulator. Five cases illustrate its operation in patients with episodes of ventricular asystole, asymptomatic changes in intraventricular conduction, a paroxysm of bigeminal rhythm, an episode of extreme nodal bradycardia, and bouts of asymptomatic paroxysmal ventricular tachycardia. In a sixth patient the instrument recorded a sudden change from a sinus rhythm at 65 to a nodal rhythm at 80 beats per minute. This sort of continuous monitoring has evident advantages over intermittent observation.

Within recent years, much attention has been given to the detection of cardiac arrest and its prompt treatment. A device has been described which will sound an alarm in the event of asystole and even automatically begin electrical stimulation of the heart.[1] However, the occurrence of cardiac arrest or ventricular fibrillation may simply represent the end-point of a long chain of unfavorable events, which may then prove irreversible. Other arrhythmias, which often portend the appearance of asystole or ventricular fibrillation, require as prompt attention and are in most instances more readily treated.

During cardiac surgery changes from normal rhythm often precede the terminal arrhythmia.[2] It is well known that Stokes-Adams episodes may be the result not only of transient asystole but also of ventricular tachycardia or fibrillation.[3] In digitalis intoxication or myocardial infarction either abnormal ventricular or supraventricular rhythms may shortly precede fatal arrhythmias. In each of these situations the prompt application of prophylactic measures and appropriate treatment may be lifesaving. Delay is often fatal and every moment of forewarning is valuable.

In addition to the changes of rhythm of serious prognostic significance, there occur annoying paroxysmal supraventricular arrhythmias of brief duration which escape identification and consequently specific treatment. More often than not, before the electrocardiograph can be found and put into operation, the arrhythmia has ceased spontaneously.

Intermittent observation of a patient by nurse or anesthetist will often result in failure to detect the presence of a transient arrhythmia or the time of onset of a more persistent one. On occasion, changes in rhythm may occur which are not readily detectable by palpation or auscultation (as idioventricular rhythms at relatively slow rates) but which may nevertheless lead to rapid circulatory collapse. Stationing a trained observer by a continuously recording electrocardiograph or oscilloscope is certainly an impractical solution in most instances.

This paper describes a cardiac monitor which is capable of detecting most significant changes in rhythm and rate, sounding an alarm, recording an electrocardiographic tracing at the time of onset of the arrhythmia, and, in some instances, administering predetermined treatment prior to the arrival of the physician.

Apparatus and Technique

The cardiac monitor is a compact, portable, single-channel, direct-writing, electronic instrument (about the size of a large table-model radio), simply built and used in conjunction with a standard electrocardiograph. The monitor receives impulses from the amplifiers of the cardiograph (fig. 1). On the basis of interpretation of these impulses it controls the motor and stylus of the cardiograph, a loud-speaker which produces an audible sound with each heartbeat, a signal device which sounds when an arrhythmia is detected, and optionally an electrical cardiac stimulator or electric valves controlling the infusion of appropriate drugs. The electrodes are taped to the patient's trunk and a long cable is used to allow for freedom of movement. Special circuits prevent patient movement and poor or broken connections from activating the device so that patients may get in and out of bed with ease. The monitor may be set to detect tachycardias (above 50 to 200 beats per minute), bradycardias (below 2 to 60 beats per minute), or the occurrence of bundle-branch block (increase in duration of QRS complex). When an arrhythmia occurs, a distinctive signal sounds (e. g., bell for bradycardia, buzzer for tachycardia) and a brief cardiographic record is written. The signal does not cease (unless turned off manually) until normal rhythm is restored, but the duration of the cardiographic record is preset and independent of the duration of the

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arrhythmia. At the onset of the next disturbance, the signal sounds again and another electrocardiographic strip is written.

Not only will arrhythmias be detected but, once the diagnosis has been established in a patient with multiple episodes of the same disturbance, therapeutic measures may be automatically initiated before the arrival of the physician. For example, in the event of asystole, but not any other arrhythmia, a stimulator circuit can be activated to apply rhythmic pulses to the chest wall, or in the event of tachycardia responding to procainamide, an infusion of this drug can be started by electrical valves controlled by the monitor. As soon as the rate returns to within the desired range, the valves stop the infusion, only to restart it should the abnormality recur. Were an arrhythmia other than tachycardia to occur, the monitor in this instance would perform its diagnostic services only and refrain from injudiciously applying therapy.

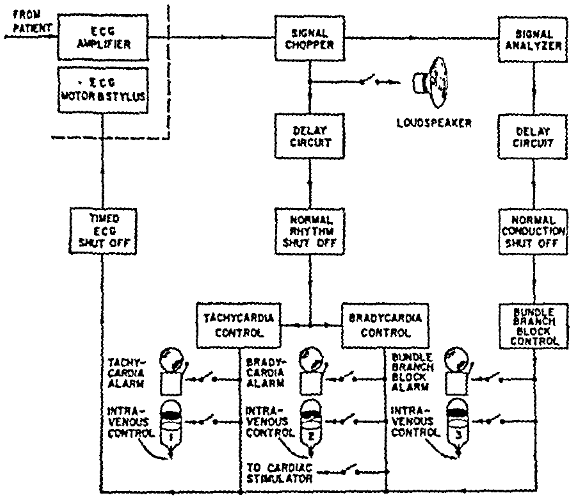

Fig. 1.—Block diagram of monitor circuits. Patient is attached to electrocardiograph. QRS pulses from the ECG amplifier are modified by signal chopper and signal analyzer so that only essential changes in configuration affect subsequent circuits and artifact potentials are eliminated. Loud-speaker may sound with each cardiac contraction. Intervals between pulses are measured in tachycardia control and bradycardia control circuits, while width of pulse is measured in bundle-branch block control circuit. Delay circuits, by averaging pulse rate and QRS duration, prevent transient disturbances from having effect, while normal rhythm and normal conduction shut-off circuits inactivate device on restoration of rhythm to prior state. Each type of arrhythmia control circuit activates different type of alarm and independent intravenous control. Bradycardia control may optionally turn on cardiac stimulator. Each arrhythmia control circuit can turn on ECG motor and stylus, duration of tracing being determined by timed ECG shut-off circuit.

Report of Cases

Case 1.—A 65-year-old woman was admitted to the Massachusetts General Hospital, Boston, on March 10, 1958, because of congestive heart failure. There was no history of syncopal episodes. Initial electrocardiogram showed normal sinus rhythm and right bundle-branch block. After being treated with digitalis and meralluride (Mercuhydrin), she had a diuresis with a 10-lb. (4.5-kg.) weight loss. Subsequent electrocardiogram showed 2:1 and 3:1 heart block. Because of the occurrence of a convulsive episode, the cardiac monitor was used. On two occasions the monitor's alarm warned of ventricular asystole (fig. 2*A*) and electrical stimulation was begun with effective results (fig. 2*B*). On another occasion a ventricular rhythm at a rate of 100 triggered the monitor (fig. 2*C*) and led to manual slowing of an intravenous infusion of epinephrine.

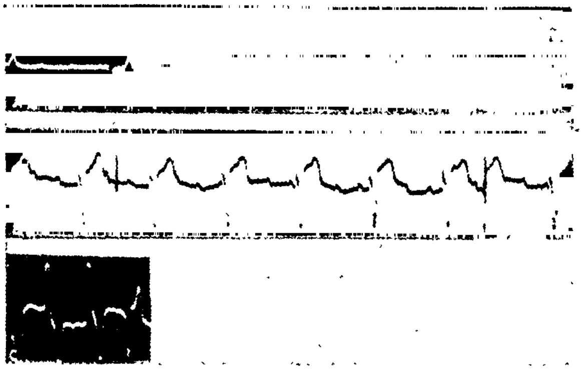

Fig. 2 (case 1).—Tracings taken automatically through monitor circuits. *A*, 3:1 atrioventricular block followed by ventricular asystole with continued atrial activity. *B*, ventricular systole in response to electrical stimulation. *C*, spontaneous ventricular tachycardia.

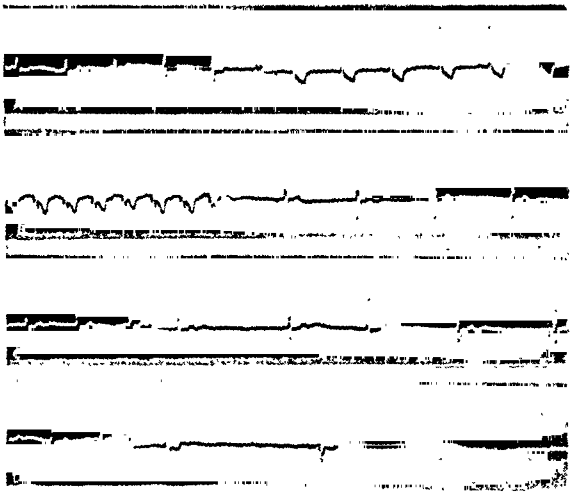

Fig. 3 (case 2).—Tracings taken automatically through monitor circuits. *A, sinus rhythm at 80 beats per minute.* Second part of tracing represents change in conduction pathway. *B*, nodal tachycardia at 120 changing to sinus rhythm at 60 beats per minute. *C*, sinus arrest with an irregular nodal bradycardia, following a faster nodal rhythm. *D*, sinus rhythm, followed by sinus arrest and then ventricular asystole.

Case 2.—A 76-year-old woman entered the hospital on April 17, 1958, because of congestive heart failure related to coronary artery disease and aortic stenosis. There was no history suggestive of paroxysmal arrhythmias. Initial electrocardiogram showed normal sinus rhythm. The patient was at first selected as a control for study of the monitor's stability. However, during a 24-hour period the monitor recorded a paroxysmal change in intraventricular conduction (fig. 3A) without change in rate, several nodal tachycardias (fig. 3*B*), a nodal bradycardia (fig. 3*C*), and sinus arrest with occasional nodal escape beats (fig. 3*D*). None of these changes in rhythm was symptomatic.

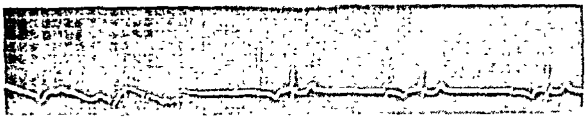

Fig. 4 (case 3).—Tracings taken automatically through *monitor circuits. Sinus rhythm is followed by bigeminal* rhythm.

CASE 3.—A 79-year-old man was hospitalized on May 11, 1958, because of symptoms suggestive of intermittent cerebral vascular insufficiency. While in the hospital he complained of brief bouts of palpitations which never occurred in the presence of an observer. An electrocardiogram was within normal limits. The cardiac monitor was attached and after several hours a record of a paroxysmal episode of bigeminal rhythm was taken (fig. 4).

CASE 4.—A 66-year-old woman was admitted on May 12, 1958, because of acute bacterial endocarditis. Initial electrocardiogram (fig. 5A) showed atrial fibrillation at an average ventricular rate of 50 beats per minute. Several hours after the monitor was instituted, the alarm sounded and the patient was found in the midst of a convulsive seizure. An electrocardiogram taken by the monitor revealed extreme nodal bradycardia (fig. 5*B*). Administration of epinephrine resulted in an increase in rate. Over the next 24 hours regular nodal rhythm at 80 beats per minute (fig. 5*C*) and a nodal tachycardia at 130 beats per minute (fig. 5*D*) were recorded by the monitor but were unassociated with symptoms.

Fig. 5 (case 4).—Tracings taken automatically through monitor circuits. *A*, atrial fibrillation, admission rhythm. *B*, extreme bradycardia. *C*, nodal rhythm. *D*, nodal tachycardia.

CASE 5.—A 58-year-old woman was admitted to the hospital on May 16, 1958, because of intermittent periods of faintness and vertigo. The initial electrocardiogram showed sinus rhythm at a rate of 65 beats per minute. Within an hour the patient's heartbeat had spontaneously converted to a nodal rhythm at a rate of 80 beats per minute, which was recorded by the monitor (fig. 6).

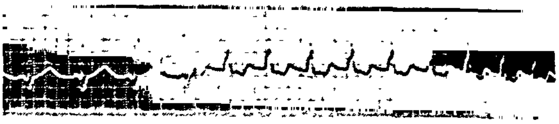

Fig. 6 (case 5).—Tracings taken automatically through *monitor circuits. Sinus rhythm at 80 beats per minute* changing to nodal rhythm at 90 beats per minute, with marked change in conduction pathway.

CASE 6.—A 61-year-old woman was admitted on June 3, 1958, with a history of complete heart block of many years' duration and occasional episodes interpreted as Stokes-Adams syncope. The electrocardiogram showed that rhythm on admission (fig. 7A) was complete atrioventricular dissociation. In the course of a 24-hour period several bouts of paroxysmal ventricular tachycardia were recorded by the monitor; none of these was symptomatic (fig. 7*B*).

Comment

These six cases illustrate that the monitor is capable of detecting not only tachycardias (cases 2, 4, and 6), bradycardias, or asystole (cases 1, 2, and 4) but also changes in the configuration of the QRS complex without significant change in rate (cases 1, 2, 3, and 5).

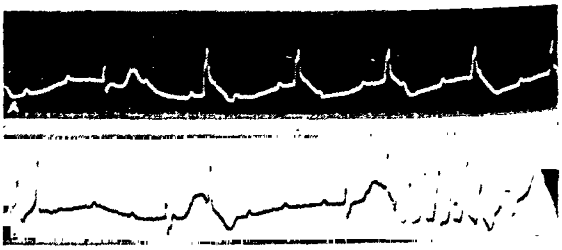

Fig. 7 (case 6).—Tracings taken automatically through monitor circuits. *A*, admission rhythm, third-degree heart block. *B*, runs of paroxysmal ventricular tachycardia.

Aside from evident application in the operating room or in instances of known Stokes-Adams syncope, it may be used to advantage in patients who complain of paroxysmal palpitations or those who are likely to develop dangerous arrhythmias. In an already present arrhythmia under treatment, the device may be used in monitoring the time of conversion to normal rhythm so that medication need not be continued longer than necessary.

Because of the stability of the circuit, it may be used with relative patient comfort for long periods. In one instance the monitor remained in place continuously for three days, during which time several moves from chair to bed or commode were made without accidental activation of the device.

Summary

A cardiac monitor used during the occurrence of significant cardiac arrhythmia will sound an alarm, cause an electrocardiograph record to be taken, stimulate the heart electrically during asystole, and cause pharmacological agents to be administered during appropriate changes in rhythm. It is believed that this device will be of value in warning of the occurrence, recording the nature, and in some instances beginning treatment of paroxysmal cardiac arrhythmias.

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SIMPLIFIED TECHNIQUE FOR SEPARATION OF CANCER CELLS FROM BLOOD

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and
Elizabeth McGrew, M.D., Chicago

The Malmgren method for the isolation of cancer cells from whole blood was simplified by substituting a centrifuge process for the filtration method of collecting cells for examination. The new method, which can be carried out in the average laboratory, produces slides of a quality comparable to those from other techniques with regard to preservation of tumor cell structure, minimal cell clumping on the slide, and adequate red cell removal from the final preparation. The Papanicolaou preparation of the slide distinguishes the malignant cell when read by a competent cytologist.

Cancer cells are often found in the blood stream of patients with malignant diseases, but only recently have laboratory techniques enabled more complete study of this phenomenon. Engell[1] reopened this field of investigation; he pointed out that malignant cells in the blood were first identified almost 100 years ago, but since that time only sporadic reports had appeared in the literature. In the course of these new studies, certain inconsistencies have arisen which require numerous observations of patients and the concurrent examination of their blood for the presence or absence of tumor cells. Because of the technical difficulties in the separation methods currently in use, requiring skilled techinicians and expensive equipment, many persons have been loath to attempt such studies. For this reason a modification of the technique first described by Malmgren and co-workers[2] has been developed by us which stresses simplicity, the use of ordinary laboratory equipment, and, insofar as possible, maintenance of the physiological state.

Review of Previous Methods

The method utilized by Engell requires the use of 2 to 5 ml. of heparinized blood from which the cellular elements are collected after centrifugation. These cells are treated with 1% saponin solution to lyse red blood cells; the remaining white blood cells and tumor cells are then coagulated with citrated plasma. These cellular "buttons" are then treated according to ordinary histological technique, mounted in paraffin, cut into serial sections, and stained with Hansen's hematoxylin and 1% aqueous eosin. The principle of this technique is hemolysis. Although this is the classic approach to the problem

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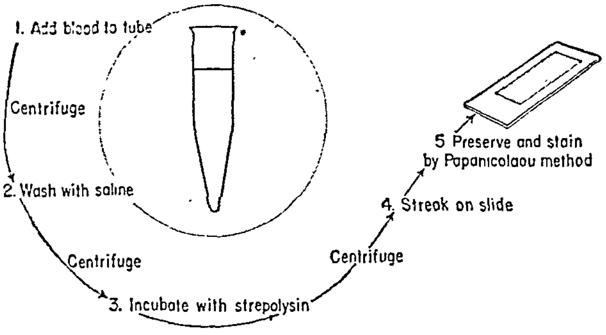
of isolation of malignant cells from the blood, the technical manipulations are considerable and the tumor cells may be damaged by the strong hemolyzing agent used.



*All samples are processed in the same 50 cc. centrifuge tube

Fig. 1.—Procedure of separation of cancer cells from blood.

A second method currently in use was developed by Sandberg and Moore.[3] This method relies on artificially accelerated sedimentation of red blood cells with bovine fibrinogen. The supernatant fluid is then centrifuged and the sedimented cells are smeared and stained with Wright's stain. The advantage of this method is simplicity, but the drawbacks make this method less acceptable than others. These disadvantages include lack of quantitation, loss of tumor cells which are carried down with the sedimented erythrocytes, and the further disadvantage that the 5-10% erythrocytes which remain form a red precipitate when stained by the Papanicolaou method.

Beginning work in July, 1956, Roberts and associates[4] developed still another method, which took advantage of the fact that tumor cells are usually lighter than the formed elements of blood. Once again heparinized blood (10 ml.) is used. Fibrinogen is added to speed sedimentation of the erythrocytes. The supernatant portion is then decanted and layered over 5 ml. of iso-osmotic albumin solution with a specific gravity intermediate between that of tumor cells and that of normal blood cells. This preparation is then centrifuged and the heavier leukocytes are spun to the bottom of the tube, while the tumor cells collect at the plasma-albumin interface. Aspiration of the cells at the interface is carried out, and they are streaked on glass slides, preserved, and stained by the Papanicolaou method. The cells which have passed through the plasma-albumin interface are similarly treated, since it was observed that many tumor cells approximated the weight of white blood cells and were found with these sedimented cells. The principal advantage of this method is that it is physiological. The cell nucleus and cytoplasm are well preserved. Its main disadvantage is that it is not quantitative. A specimen negative for tumor cells does not mean that cells are absent, since many tumor cells are lost in the initial sedimentation of erythrocytes.

The method developed by Malmgren and associates[2] is a combined enzymatic and filtration method. Each blood sample (20 ml.) is washed with saline solution to remove naturally occurring antistreptolysin. The sample is then treated with streptolysin O, which lyses the erythrocytes and the polymorphonuclear leukocytes. After this, the remaining lymphocytes and tumor cells are resuspended in saline solution and filtered through a fine (5 μ) filter. The filters are then stained and mounted on large glass slides for examination. Filtration requires the use of an apparatus for creating negative pressure. The most obvious advantage of this method is quantitation. The advocates of this method have shown 100% recovery of counted cells. Also, a human tumor established in tissue culture was added to a blood sample and reseparated by this method. It was then successfully reimplanted—thus demonstrating viability of the tumor cells.

In our hands, however, this method has presented several difficulties. Filtration is technically difficult and unpredictable. Some samples are easily filtered, while others require much time and many filter changes. Cells are often distorted in the interstices of the filter by the pressure required for filtration. Microscopically, the filters are "wavy," as

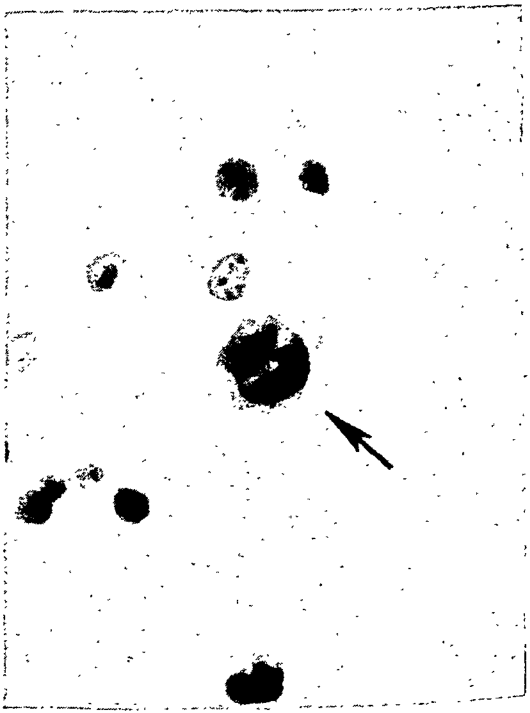


Fig.2.—Photomicrograph showing epidermoid carcinoma of penis (×1,100).

there is much background debris, making examination of the slides difficult. Also, the streptolysin O added to lyse the susceptible cells is hyperosmolar. (Made up with buffered solution, the streptolysin O solution is 790 milliosmols [mOsm.] per liter.)

Collection of Samples

As has been done in previous work reported from this laboratory, samples are collected from a variety of sources. These include peripheral (antecubital vein) catheter samples from large veins draining the general tumor area (inferior vena cava, axillary vein, etc.) and samples from veins directly draining the tumor (renal vein, mesenteric vein, etc.).

Method

We have modified Malmgren's method[2] with use of streptolysin O but rely on centrifugation rather than filtration to isolate the cancer cells; this is a very simple procedure and can be carried out without elaborate laboratory facilities; moreover, highly trained technicians are not required for this method. In the course of handling a blood sample there are only two procedures requiring the transfer of the sample from one container to another; these are the change of the blood sample from the syringe to a centrifuge tube and the transfer of the remaining tumor and white blood cells to glass slides. All steps concerning the actual lysis of red blood cells and polymorphonuclear leukocytes are carried out in the same 50-ml. conical centrifuge tube. This tube and the collecting syringes are siliconized with one of the standard materials generally available. A water bath, a centrifuge capable of 1,000 rpm, and ordinary glass microscope slides complete the necessary physical items. Reagents necessary are streptolysin O, isotonic sodium chloride solution, and distilled water. The general procedure is outlined in figure 1, and the detailed steps are given below.

1. Whole blood (10 ml.) is collected in a siliconized syringe and transferred to a 50-ml. siliconized conical centrifuge tube. These tubes contain 1 mg. of heparin in 0.1 ml. of solution.
2. The sample is centrifuged at 1,000 rpm for 20 minutes.
3. The plasma is decanted and 15 ml. of isotonic sodium chloride solution is added and mixed. The sample is recentrifuged for 20 minutes as before.
4. Once again the supernatant fluid is decanted and 15 ml. of saline solution is added, mixed, and centrifuged for 20 minutes. These washings are performed to remove the naturally occurring antistreptolysin.
5. Three 10-ml. vials of streptolysin O reagent (Difco Laboratories, Detroit) are prepared with use of 9 ml. of distilled water per vial. This must be used within 10 minutes. With most lots of streptolysin O this has resulted in a solution containing 280 mOsm. per liter.
6. The supernatant fluid of the last washing (step 4) is decanted, the three vials of streptolysin O are added, and the tube with its contents of enzyme and sedimented cells is incubated in a water bath at 39 C for 10 minutes. The contents are agitated gently during this incubation.
7. After incubation, the tube is centrifuged for 10 minutes at 1,000 rpm.
8. The supernatant fluid is decanted and 10 ml. of isotonic sodium chloride solution is added, the tube being once again centrifuged for 10 minutes at 1,000 rpm. This washing is to remove cell debris.
9. The supernatant fluid is decanted and the sediment placed on 12 ordinary glass slides and fixed immediately in ether-alcohol solution. These slides are stained by the Papanicolaou technique.[5]

Fig. 3.—Photomicrograph showing undifferentiated malignant retroperitoneal tumor (× 1,100).

10. Scanning is performed.
11. Confirmation by a trained cytologist is indicated.

Results

From a cytological standpoint the preparations obtained by this method have been satisfactory (fig. 2 and 3). There is a background of lymphocytes with a few polymorphonuclear leukocytes. It is sometimes possible to place the sediment on fewer than 12 slides, while at other times more will be necessary—the important consideration being a thin smear which makes the formidable process of scanning more reasonable. Most of the cells have been single, although some clumps have been identified. Some apparent tumor cells are stripped of their cytoplasm. We have also observed a number of large cells with a lobulated nucleus. These at first appear to be malignant cells, but further study has indicated that these are megakaryocytes—not malignant cells. Figure 4 shows such a cell which was identified in the peripheral blood of a patient with preinvasive carcinoma of the uterine cervix. Also shown in figure 4 is a megakaryocyte from the marrow of a "normal" patient for comparison. Both have been stained by the Papanicolaou method.

Viability of cells processed by this method has been shown by treating a suspension of Walker-256 carcinosarcoma cells by the above method and then injecting the suspension subcutaneously into rats. Four of 10 rats so injected developed tumor "takes." The usual "take" is 100%.

As stated previously, the method as described is extremely simple and can be carried out without elaborate equipment. In addition, the number of positive samples in 100 patients is about twice that revealed in our "interface" method. However, since the number of various types of cancer in this series is comparatively small, we are not reporting the actual percentage figures at this time.

Summary

A method of isolating cancer cells from the peripheral blood has been developed which is a modification of a method previously described but is much simpler. Our preliminary experience with it indicates that it compares favorably with other methods as far as quantitation is concerned. Its main advantage is that it is a technically easy method requiring only reagents and equipment available in most laboratories. The ever-present burden of careful scanning cannot be avoided, and the availability of a competent cytologist for positive identification of malignant cells is still essential.

840 S. Wood (12) (Dr. Long).

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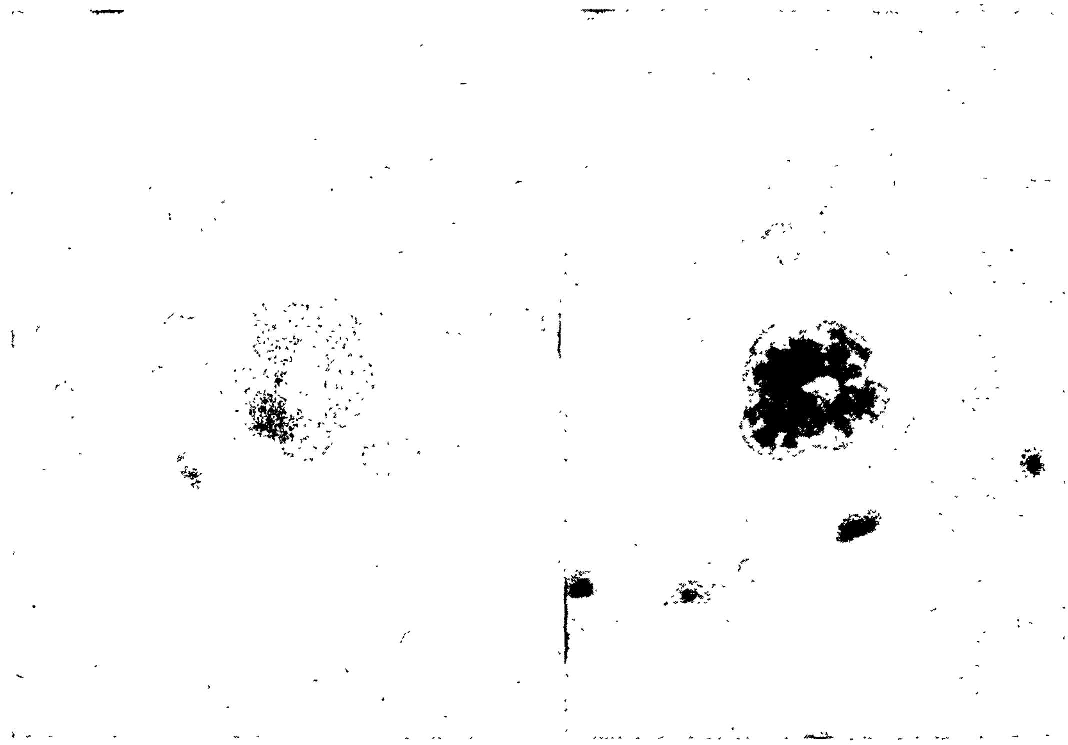

Fig. 4.—*Left,* megakaryocyte from bone marrow of "normal" patient. *Right,* cell believed to be megakaryocyte isolated from peripheral blood of patient with preinvasive carcinoma of cervix (×1,100).

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INCIDENCE OF CHOLECYSTITIS AND OTHER DISEASES AMONG PIMA INDIANS OF SOUTHERN ARIZONA

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Among 2,688 Pima Indians above the age of 15 years there were 125 hospital admissions for cholecystitis during a two-year period. During that same period only three cases of myocardial infarction were definitely diagnosed, no patient was treated for angina pectoris, and no case of peptic ulcer was reported. The average Pima Indian was found to consume 2,800 calories daily, and fats comprised 24% of the calories intake, with 87% being animal fat; lard was used almost exclusively as a cooking fat. Meat and vegetables were usually eaten about once a week. The role of diet in the etiology of the disease pattern among Pima Indians is consistent with current thinking as to the pathogenesis of degenerative heart disease.

It is well known to physicians working on Indian reservations in the Southwest that there is a relatively high incidence of gallbladder disease and low incidence of arteriosclerotic heart disease and peptic ulcer among southwestern Indian tribes. Lam,[1] in 1954, reported that gallbladder disease accounts for 3.6% of all hospital admissions and is the most frequent surgical condition encountered among the Sioux Indians. Gilbert,[2] in 1955, reviewed 10,267 Navaho Indian hospital admissions and reported 125 admissions for gallbladder disease and only 5 admissions in which coronary thrombosis was suspected (in none of these was it proved). No further reference to the incidence of these diseases is encountered in the medical literature. The present study reports the incidence of cholecystitis, arteriosclerotic heart disease, and peptic ulcer among the Pima Indians from the time (July, 1955) when the U. S. Public Health Service assumed responsibility for the medical care of the American Indian.

The Pima Indians live on a 372,000-acre reservation in the southern Arizona desert. They have accepted many of the white man's ways, especially modern medicine. Tribal medicine is almost extinct among the Pimas,[3] in contrast to many other southwestern tribes in which many diseases are treated by medicine men, making a statistical report almost impossible. The Pimas receive their medical care exclusively at the PHS Indian hospitals at Sacaton and Phoenix, Ariz. This report is an analysis of the records of these two hospitals over the two-year period from July, 1955, to June, 1957. The proportionate age groups of the tribe were obtained by estimates made from the 1950 U. S. census report.[4]

Findings

Gallbladder Disease.—There were 125 admissions for cholecystitis during this two-year period. These came from a population of 4,668,[4] of which 2,688 are above the age of 15 years and in the cholecystitis-susceptible age group. Out of every 100 Pima Indians above the age of 15, 2.3 were admitted yearly because of gallbladder disease. Admissions were for severe acute cholecystitis or for recurrent chronic cholecystitis with acute exacerbation of the disease. Patients with mild cases of cholecystitis were treated as outpatients and were not included in this study. The diagnoses were established on the basis of clinical history and physical examination and were supported by abnormal cholecystograms in 92% of the 125 admissions in this group.

Persons in all age groups between 20 and 70 years were approximately equally affected, with a preponderance in the sixth decade. There was a relatively high frequency in females below the age of 30. The incidence of cholecystitis is seven times higher in the female than the male (see table).

The incidence of diabetes in patients with cholecystitis was 12.5%. This compares to an incidence of 11.6% among all Pima Indian hospital admissions, suggesting that, while there is a relatively high incidence of diabetes among the Pimas, cholecystitis does not seem to be related to it. A history of cholecystitis in the immediate family was obtained in 34% of all patients with gallbladder disease. Cholecystectomy was performed in 74 patients during the two years, 18 of whom required exploration of the common duct.

Gallbladder carcinoma was found during operation in two Pima Indians. Of patients from all tribes admitted for cholecystitis to these two hospitals, 8 were found to have carcinoma of the gallbladder out of 273 admissions for cholecystitis—an incidence of 2.9%. Carcinoma of the gallbladder was the most common form of cancer seen in these two hospitals during the two years.

Arteriosclerotic Heart Disease.—There were three cases of myocardial infarction definitely diagnosed among Pima Indian admissions during the two years. One other patient had a clinical course suggestive of myocardial infarction but showed only a left bundle-branch block. Two other Pima Indians

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were suspected of having myocardial infarction, though the history was difficult to obtain and the patients died aged 78 and 90, respectively, before an electrocardiogram was recorded.

No patient was treated for angina pectoris at the Sacaton hospital during the two years studied. During 1956, there were only 12 cases of coronary thrombosis diagnosed among the 23,000 southwestern Indians cared for by the Phoenix area office of the U. S. Public Health Service.

Peptic Ulcer.—There was no case of peptic ulcer reported among the Pima Indians in these two years. Among all tribes treated at the PHS Indian hospital at Phoenix, averaging 8,500 admissions annually, only 2 cases of duodenal ulcer, proved by x-ray, were found during the two-year period. Two other patients with a clinical history which suggested peptic ulcer had a normal gastrointestinal series. In 1956 five cases of peptic ulcer were diagnosed among the 23,000 southwestern Indians under the jurisdiction of the Phoenix area office.

Comment

The high incidence of gallbladder disease and the low incidence of arteriosclerotic heart disease and peptic ulcer in a relatively inbred tribe is difficult to explain on the basis of the currently suspected etiology of these diseases. The findings among the Pima Indians are consistent with the findings of Lam [1] among the Sioux Indians and Gilbert [2] among the Navaho tribe. The low incidence of peptic ulcer in an Indian tribe has not been previously reported.

Surgical facilities were inadequate in previous years to meet the demand for elective gallbladder operations, so that conservative treatment for cholecystitis was commonly prolonged. This may account partially for the high incidence of recurrent acute exacerbations of chronic cholecystitis and for the relative frequency of carcinoma of the gallbladder.

Other contributing factors may be the heavy body build with a tendency toward obesity found among Pima Indians. The role of diet in the etiology of this disease pattern is difficult to evaluate. A diet study of Pima Indians shows their basic food to consist of beans, tortillas, and coffee, with hot chili peppers a commonly used side dish. Meat and vegetables are usually eaten about once a week, due to lack of funds and lack of storage facilities for perishable foods. The average Pima Indian consumes 2,800 calories daily. This contains 105 Gm. of protein, of which only 16% originates from animal sources. Fats comprise 24% of the calorie intake, with 87% being animal fat. Most foods are fried in lard, which is used almost exclusively as a cooking fat.[5]

It is conceivable that the quantities of fried and spicy foods eaten regularly by Pima Indians may aggravate existing cholecystitis. The low incidence of coronary disease among these Indian groups in view of the relatively low-fat diet is consistent with the findings of Keys [6] in other population groups where a low fat intake was proportional to a low incidence of degenerative heart disease.

The rare occurrence of peptic ulcer among the Pimas and other Indian tribes may be due to the relatively low stress and noncompetitive nature of Indian communal life. It will be interesting to note any future changes in this disease pattern as the Indian is assimilated more into the competitive society of the United States.

Summary

A study of the incidence of gallbladder disease, arteriosclerotic heart disease, and peptic ulcer among the Pima Indians of southern Arizona was facilitated because the Pima is one of the few tribes that has completely accepted modern medicine; the statistical evaluation is, therefore, reasonably valid. In a population of 2,688 Pima Indians above the age of 15 years, 125 were admitted over a two-year period for gallbladder disease. The occurrence of cholecystitis is seven times more frequent in the female than in the male. Eight cases of carcinoma of the gallbladder were found among 273 admissions for gallbladder disease; this was the most common form of cancer seen. Three cases of myocardial infarction were diagnosed among Pima Indian admissions during the two years; no patient with angina pectoris was encountered. The low incidence of arteriosclerotic heart disease is interesting in that these Indians eat a relatively low-fat diet. No patients with peptic ulcer were seen during this same period.

Incidence of Cholecystitis According to Age and Size of Population Among Pima Indians, 1955-1957

Age, Yr.	Population	No. with Cholecystitis			Rate per 100 Population
		Male	Female	Total	
15-19	428	0	4	4	0.9
20-29	620	2	31	33	5.3
30-39	475	2	23	25	5.3
40-49	432	1	17	18	4.2
50-59	306	7	23	30	9.8
60-69	250	3	10	13	5.2
70+	177	0	2	2	1.1
Total	2,688	15	110	125	4.6

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ELECTROSHOCK THERAPY AND TRANQUILIZING DRUGS

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Electroshock therapy (EST) was used in 170 patients whose mental illness had not been ameliorated by intensive treatment with tranquilizing drugs. All of these patients were incapable of social or vocational activity before the EST and were rated 1 (lowest) on a 4-point scale. In another group of 131 patients the EST was given while the administration of tranquilizers was continued. Of the 170 patients, 117 (69%) had satisfactory results with EST, as measured by higher ratings on the scale. Simultaneous use of tranquilizers with EST did not reduce the number of EST treatments needed for good results, decrease apprehensiveness before treatments, or shorten the postconvulsive psychoses; neither did it increase the risks of EST. It did help in the management of agitated patients. It is therefore recommended only when specifically indicated in a given situation.

Determination of the relative merits and effectiveness of the tranquilizing drugs, as compared to electroshock therapy, in the management of certain types of psychiatric disorders is a controversial matter in present-day psychiatry. Some physicians maintain that electroshock therapy in combination with use of various tranquilizing drugs is more effective than electroshock therapy alone.[1] Others warn that this technique is fraught with danger.[2] The following observations are a summary of my experiences in this field during the past four years.

All the patients in these series were seen in private practice. They all received electroshock therapy in a hospital setting on either an inpatient or an outpatient basis, and they all had complete general and neurological examinations at the time of the initial visit. All patients over 35 years of age had electrocardiograms and chest x-rays prior to the electroconvulsive therapy (ECT). Laboratory studies were performed if indicated. In all but a few of the patients the ECT technique was to put the patient in a light sleep with intravenous administration of thiopental (Pentothal) sodium and then to administer succinylcholine (Anectine) chloride intravenously. The electric current was delivered with use of a standard unit, 50 seconds after the injection of succinylcholine.

Method of Evaluating Level of Improvement

The technique used in evaluating the level of improvement was the same as that explained by me in previous publications on various therapeutic methods.[3] It considers and attempts to quantify, whenever possible, both subjective and objective factors. The criteria used stress the patient's adaptation to routine responsibilities of everyday life in addition to the degree of symptomatic improvement. The degree of pride and pleasure derived from successful performance was also considered. This is a rather strict technique of evaluation and presupposes that the patient has been facing the routine responsibilities of everyday life. In detail, the factors evaluated were as follows:

Performance.—Vocational performance was considered (1) excellent if the patient held full-time employment, functioning efficiently without strain and taking great pride and pleasure from attainments; (2) good if he held full-time employment, functioning with greater effort than was necessary prior to illness and taking moderate pride and pleasure from attainments; (3) fair if he was employed intermittently, functioning with considerable difficulty and frequently absent with faulty performance at times and lack of pride and pleasure; and (4) poor if he was unable to perform at all.

Social performance (individual and group interpersonal relationships) was considered (1) excellent when his social performance was active and comfortable with a high level of pride and pleasure obtained; (2) good when it was active but with slight to moderate difficulty at times and with limited pleasure capacity; (3) fair when he socialized with great difficulty, readily became anxious, and had a lack of pride and limited and infrequent pleasure; and (4) poor when his behavior was seclusive or his relations were chaotic.

Amelioration of Anxiety.—Second, the patient's anxiety and its degree of amelioration were measured. Anxiety is defined here in its broadest aspect. I consider it synonymous with fear, whether this fear is generated by unconscious conflict or actual difficulties, and I attempted to quantify anxiety according to a four-point scale after analyzing this psychophysiological phenomenon into several components; namely, motor, affectual, verbal, and autonomic. The scale was as follows: (1) calm, no restlessness, overt expression of fear, when it occurred, appropriate to the severity of the actual stress; (2) slight restlessness, slight affectual expression of fear, slight pressure of speech; (3) marked

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restlessness, pacing, marked overt affectual expression of fear, often severe pressure of speech; and (4) panic.

Amelioration of Initial Symptoms.—The third criterion, degree of amelioration of initial symptoms, was also marked on a four-point scale, as follows: (1) excellent, all symptoms completely gone; (2) good, symptoms markedly reduced in intensity and frequency, patient able to cope with them; (3) fair, slight improvement only with the symptoms continuing to plague patient most of the time and with marked impact; and (4) poor, symptoms unchanged.

Dreams.—Whenever possible, dreams were sought out and studied in an attempt to gain additional information. Disappearance of nightmares, decrease in the frequency of rage dreams, and increase in the frequency of pleasant dreams were points evaluated.

Final Improvement Rating.—The final improvement rating, on a four-point scale, took into account all factors described above: (1) excellent: full-time efficient employment, active and comfortable in social performance, marked pride and pleasure from vocational and social performance; (2) good: full-time employment but requiring slightly greater effort than usual, active socially but with slight to moderate difficulties at times, slight residual anxiety, symptoms markedly reduced in intensity and frequency, limited pride and pleasure from performance; (3) fair: working but with considerable difficulties and frequent absences, socializing with great difficulty, moderate to marked residual anxiety, slight improvement in symptoms but minimal pride and pleasure from performance; and (4): poor, unable to perform vocationally or socially, anxiety level severe and unchanged, symptoms unchanged, absence of pride and pleasure from performance.

Electroshock Therapy After Failure of Intensive Drug Therapy

I treated with electroshock therapy 170 severely ill patients who were first exposed to intensive treatment with various tranquilizing drugs. Prior to the onset of electroshock therapy all were very ill, unable to perform vocationally or socially in addition to being plagued by disturbing symptoms. There were 108 women, ranging in age from 22 to 74 years, and 62 men, from 25 to 71 years of age. There was a broad range of diagnosis of psychotic illnesses commonly seen in active neuropsychiatric practices and in clinics; 94 patients had schizophrenia, of whom 33 were classed as mixed; 20, catatonic; 20, depressed; 12, pseudoneurotic; and 9, paranoid. Sixty-one had involutional melancholia; 11, organic psychoses; and 4, manic-depressive psychoses.

The duration of illness in this group of patients prior to their electroshock treatments ranged from three weeks to eight years, most of them having been very sick for from one to eight months. Therapy with phenothiazine derivatives was administered for at least two weeks and with reserpine for a minimum of three weeks before institution of electroshock therapy. Some workers, especially those in large public institutions, will claim that these periods are not long enough in some instances to test the efficacy of the tranquilizers. I would answer this claim with the facts that those patients who were switched to electroshock therapy after two to three weeks of therapy with tranquilizers were becoming much worse and were in many instances a danger to themselves or to the community. Second, it was my experience with the phenothiazines [3a] that if they did not begin to produce definite results during the first few weeks of treatment, providing the dosages were in the higher range, the chances for effective results were poor. Similar results have occurred with the use of reserpine in private practice; if definite benefit is not noted in three weeks there is little likelihood of any significant changes from the drug.

The patients had received a variety of the more popular tranquilizers; 89 were receiving therapy with chlorpromazine hydrochloride; 58 with promazine hydrochloride; 57 with prochlorperazine; 40 with perphenazine; 45 with reserpine; and 68 with meprobamate. As will be noted from the figures many patients had received two or more drugs before electroshock therapy was instituted.

Those patients given chlorpromazine or promazine received the drug for a minimum of two weeks at maximum dosages of 600 mg. per day. Those given prochlorperazine received the drug for two or more weeks, the maximum daily dose being 125 mg. Patients given perphenazine remained on the drug for two or more weeks, the maximum daily dose being 64 mg. Those on reserpine were treated for a minimum of three weeks, and the maximum daily dose was 5 mg. Twenty-six patients received combined treatment with reserpine and chlorpromazine. In addition, 68 patients had received treatment with meprobamate ranging from 3,000 to 8,000 mg. per day.

In spite of drug therapy these patients remained unable to perform vocationally or socially. Before electroshock was instituted drug therapy was discontinued for 48 hours in the case of the phenothiazines and 72 hours for reserpine. Most patients had not had drug therapy for a week. The patients received from 5 to 18 electroshock treatments (EST), the average being 8. Each patient served as his own therapeutic control. Of the 170 patients 69 (41%) improved under electroshock therapy to the point of improvement rating 1; 48 (28%) to the point of rating 2; 21 (12%) showed the slight improvement of rating 3; and 32 (19%) remained unchanged (rating 4).

Of 170 patients 117 (69%) achieved improvement ratings 1 and 2; that is, they improved to the point of being able to function socially and vocationally on a high plane of efficiency and with a marked degree of pride and pleasure. Only those persons who continued to function at these levels for a minimum of three months were included in groups 1 and 2. The table shows level of improvement related to type of illness. It will be noted that 83% of those who were diagnosed as having involutional depressions had very good results and were included in groups 1 and 2, as compared with 65% of the schizophrenic patients. Analyzing the results further I found that of the 53 patients who failed to respond to electroshock therapy 39 had been ill for more than a year. The time relationship is striking when it is noted that 26 of the 33 schizophrenic patients who were therapeutic failures had been acutely psychotic for more than a year and were severely regressed.

Another group of 86 patients, who had obtained only transient improvement from electroshock treatments administered by other psychiatrists, was also reviewed. They were treated intensively with several of the phenothiazine derivatives (i. e., 66 patients given up to 1,000 mg. of chlorpromazine per day; 9, up to 1,000 mg. of promazine; 6, up to 250 mg. of prochlorperazine; and 4, up to 80 mg. of perphenazine. Nineteen (23%) of these patients responded very satisfactorily, and 37 of the remaining 66 responded to subsequent series of electroshock.

Electroshock Therapy in Combination with Tranquilizing Drugs

A total of 131 patients were treated with electroshock therapy in combination with tranquilizing drugs as follows: 123 had EST in combination with phenothiazine derivatives, of whom 96 had chlorpromazine; 12, promazine; 9, prochlorperazine; and 6, perphenazine; 4 had EST in combination with reserpine; and 4, in combination with meprobamate. All patients had been treated intensively with one or more of the above-named drugs without significant improvement, and all were severely ill. Eighty-seven were women ranging in age from 21 to 73 while 44 were men, aged from 22 to 69. There were among them 78 patients with schizophrenia, of whom 33 were classed as mixed; 16 as depressed; 15, pseudoneurotic; 8, catatonic; and 6, paranoid. There were 49 patients with involutional depressions, 2 with manic-depressive psychoses, and 2 with organic psychoses. Sixty-two of the patients had had EST previously. The duration of illness in patients in this series prior to the onset of combined treatment ranged from five weeks to 10 years, most patients having been very ill for from six weeks to 10 months.

The therapeutic technique was as follows: The patients continued to take the same total daily dose of a tranquilizing drug as they had prior to the onset of EST. The daily doses of the phenothiazines during EST ranged from 200 to 800 mg., with an average dose of 500 mg. for chlorpromazine and promazine; from 60 to 175 mg., average dose 100 mg. for prochlorperazine; and from 24 to 64 mg., average 48 mg. for perphenazine. The daily doses of reserpine ranged from 2 to 15 mg., average dose 6 mg.; and the daily doses of meprobamate ranged from 1,600 to 4,800 mg., average 2,000 mg. Premedication with intravenously given thiopental and succinylcholine was routine. A total of 1,024 combined treatments was given. The individual series ranged from 4 to 21 treatments, with the average about 8.

In general, in our experience, there was no significant advantage in using electroshock therapy in combination with the phenothiazine preparations over routine electroshock therapy by itself, except in a few limited situations that will be pointed out. In this, the impression of others[1] that combined treatment with ECT and chlorpromazine reduces the total number of treatments required for good results was not confirmed. If one reviews the literature on this point one gathers that there is no convincing statistical documentation to substantiate the impressions of the authors. I found the average number of treatments per patient with combined therapy to be the same as for a group of 150 patients, with similar diagnoses, treated with EST alone.

Improvement with Electroshock After Failure of Drug Therapy Related to Type of Psychosis in 170 Patients

Original Diagnosis	No. of Patients	Improvement Rating							
		1		2		3		4	
		No.	%	No.	%	No.	%	No.	%
Schizophrenia	94	29	31	32	34	16	17	17	18
Involutional melancholia.	61	38	62	13	21	4	7	6	10
Manic-depressive psychoses	4	2	50	1	25	1	25	..	..
Organic psychoses	11	..	..	2	9	..	..	9	91
Patients, total no.		69		48		21		32	

The improvement ratings with combined therapy were statistically very close to the ones obtained with EST alone. We found that 94 (72%) of the 131 patients treated by the combined technique were able to function socially and vocationally as they had prior to the onset of their psychoses. The breakdown as for the group treated with EST alone was as follows: 41 (31%) of the 131 patients achieved an improvement rating of 1; 53 (41%) a rating of 2; 19 (15%), 3; and 18 (13%), 4. There were no specific benefits from combined treatment for patients with schizophrenia or agitated depressions. As with all other therapies the more chronic the illness the poorer the results. This study could not confirm the impressions of those who claimed that combined therapy was superior to EST alone in the treatment of the chronic psychoses.[4]

I did not find that there was any lessening of the painful anticipation and anxiety that so often precedes electroshock therapy with the combined phenothiazine-EST technique, nor could I confirm the impressions of some[5] that EST in combination with the tranquilizing drugs decreased or in any way abbreviated postelectroconvulsive organic psychoses.

There are, however, several specific instances in which combined therapy is of definite benefit. The first is in the management of some wildly agitated psychotic patients, such as may be seen among those who have catatonic schizophrenia or agitated depressions, and in the management of the now rather rare but severe manic phases of manic-depressive psychosis. If parenterally administered chlorpromazine or promazine fails to tranquilize the patients sufficiently, intense daily EST remains the preferred treatment. I did not find that therapy with phenothiazine and EST shortened the time required to relieve these states effectively, but intravenous and/or intramuscular administration of chlorpromazine or promazine given at intervals between shock treatments in some instances rendered the patient more manageable during the first few days. Combined therapy was also of help in managing those patients who became agitated during the EST series. Parenterally given phenothiazines may be effective in keeping the patient relatively calm between the electroshock treatments.

Combined therapy may be of benefit in yet another instance. It is of definite help as maintenance therapy in some psychotic patients who obtain only transient or incomplete remissions from EST or drug therapy alone. Electroshock treatments at intervals of several weeks plus oral therapy with phenothiazines have enabled us to keep a few chronically ill patients functioning vocationally and socially, though admittedly on a marginal level, whereas without such therapy they would have required long-term institutionalization.

Finally, although it is not, strictly speaking, "combined therapy," the phenothiazines are of definite help in controlling the agitation and restlessness that often accompany the organic psychoses which commonly follow a series of electroshock treatments for a period of one or two weeks.[6] If the agitation does not subside by then, further EST is indicated.

Complications of Combined Therapy

I have not found combined therapy with phenothiazine and EST to be any more difficult to manage or more dangerous than EST alone. This is in accordance with the findings of other observers.[1a] It did not prolong post-EST apnea, nor was it associated with untoward hypotensive reactions. There was no evidence of potentiation with the intravenously administered thiopental or succinylcholine.

There was only one severe complication in a patient receiving combined therapy. This was a poor-risk, severely depressed patient who was treated after other techniques failed. The patient was 63 years of age and had chronic auricular fibrillation which for the most part was controlled by quinidine therapy; he had had three transient hemiparetic episodes due to emboli and was being given anticoagulant therapy. Because high dosages of chlorpromazine, promazine, and reserpine, singly and in combination, had failed (these were the drugs available at the time), and because the patient's strong suicidal drives were a constant threat, after continued consultation with cardiologists it was decided that electroshock should be instituted. No difficulties were encountered during the first seven combined treatments. In the course of his eighth treatment he developed cardiac arrest of sufficient duration to cause cortical and subcortical dysfunctioning that fortunately cleared. This complication cannot be attributed specifically to the use of the combined therapy, as it could just as readily have occurred in this type of poor-risk patient with EST alone.

My experience with combined therapy with EST and reserpine and EST and meprobamate is not sufficient to draw conclusions from. EST-reserpine therapy was not stopped because of any untoward complications, but rather because reserpine in general was found to be too cumbersome for use in ambulant patients. Similarly, use of the meprobamates in psychotic patients has been all but discontinued, since beneficial results with this drug have been very infrequent.

Although there are a number of published reports attesting to the dangers of combined EST-chlorpromazine and EST-reserpine therapy, they do not include any well-documented large series of cases in which the physical status of the patients was studied and documented prior to therapy. On the other hand Ayd,[1a] after canvassing 179 psychiatrists, found that almost 400,000 combined treatments were given with either EST and chlorpromazine or EST and reserpine without significant difficulties being incurred.

In evaluating our statistics and results one should keep in mind that most of the patients described here were ill for a relatively short period of time as compared with patients studied in large public institutions. Very few showed any deterioration. Also, since all were seen in private practice or on outpatient bases, our criteria for improvement, as mentioned above, depended primarily on the degree to which the patient was able to resume functioning vocationally and socially and how much pride and pleasure was associated with this performance. Therefore, in comparing our findings with other reports on the relative effects of the tranquilizers as compared with EST or of the relative advantages of combined therapy with tranquilizers and electroshock, it would be necessary to compare the following points: (1) whether the patients reviewed were inmates of state hospitals or patients seen in private practice or on an outpatient basis; (2) the duration of illness and degree of regression or deterioration; and (3) the criteria established for estimating the degree of improvement.

Summary

Failures with intensive phenothiazine, reserpine, or meprobamate therapy do not, by any means, rule out the possibility of obtaining good results in psychotic patients for whom electroshock therapy (EST) is indicated. Of 170 psychotic patients who failed to benefit from the tranquilizing drugs 69% had satisfactory results with EST. Combined therapy with phenothiazines and electroshock, in general, neither reduced the total number of electroshock treatments required for good results, decreased the degree of pre-EST apprehension, nor shortened the postconvulsive organic psychoses.

Parenterally given phenothiazines are helpful in managing some of the more agitated or manic patients in the intervals between electroshock treatments during the first few days of therapy. They also may be of aid in calming the agitation that may occur during an EST series and in the management of the agitation and restlessness associated with the post-EST organic psychoses.

Combined therapy, in my experience, carries no greater risk than EST alone. I did not find it necessary, in general, to discontinue the phenothiazine drugs before starting EST. I do not recommend the routine use of electroshock therapy in combination with the phenothiazines, because it was not found to be more advantageous than EST alone, except in a few specifically designated instances.

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CHOICE OF ANESTHETIC AGENT.—The idea of specific choice of anesthesia or anesthetic agent has been based upon two rather broad concepts. The first of these is that certain disease states require or are harmed less by a certain type of anesthetic agent. The second is that there exist certain rather definite contraindications and indications for each particular anesthetic agent. . . . These concepts are not valid. . . . Evidence for my stand on this matter is the fact that many clinics and practicing groups have widely varying choices of anesthetic techniques and management with no apparent difference in results. Such would hardly be the case if there were one definitely superior method or one superior agent to be used. . . .

The common concept that heart disease contraindicates the use of cyclopropane is based upon the belief that arrhythmias are due to the toxic effect of the agent. . . . These undesirable events are due either to overdose of the agent, which can hardly be blamed on the agent itself, or to hypoventilation or asphyxia occurring concurrently with the administration of the agent. One might look at the cyclopropane question in another way and ask: What better agent for a sick heart could one desire than one which is rapid, not unpleasant, very flexible, offers a minimal excitement phase, and probably offers less depression of myocardial function for a given level of central nervous system depression than other inhalation agents? —W. K. Hamilton, M.D., Fallacies in Choice of Anesthetic Agent, *Transactions of the American Academy of Ophthalmology and Otolaryngology*, March-April, 1959.

CHLOROTHIAZIDE—A SURVEY OF ITS EFFECTS IN HYPERTENSIVE PATIENTS

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A definite hypotensive effect from chlorothiazide was observed in 80% of 65 patients studied. This was more pronounced in those with severe hypertension and in those receiving ganglionic blocking agents. Of the 23 patients who had formerly required ganglionic blocking agents, 12 were able to discontinue that therapy. It would seem that periodic determinations of the serum potassium level are necessary in any patient who is receiving chlorothiazide on a long-term basis. Twenty-eight patients (43%) in this group showed a drop in potassium level to 3.5 mEq. per liter or below. This occurred in 12 despite the concurrent administration of 2 to 3 Gm. of potassium chloride daily. It is now well recognized that renal lesions may accompany potassium deficiency in man. Symptoms of this may be minimal and their onset insidious. There is also danger of hypokalemia potentiating digitalis poisoning.

Chlorothiazide (Diuril) is a potent drug in the treatment of hypertension and is now one of the most widely used drugs for that purpose. The drug produces a hypotensive effect only in hypertensive persons,[1] but its mode of action is still unknown. It also has diuretic and saluretic effects. Moyer and associates [2] have suggested that through its diuretic action total blood volume is decreased—thereby potentiating the effect of ganglion blockade. These authors noted no significant reduction in blood pressure when this drug was administered to a group of patients who had never received blocking agents. Freis and co-workers,[3] however, noted that, in addition to its potentiating action of ganglionic blockade, chlorothiazide is a hypotensive agent in its own right. They measured the effect of chlorothiazide in 10 previously untreated, hospitalized patients without edema in whom basal blood pressure readings were obtained for six days before the administration of 1.5 Gm. of chlorothiazide daily for six days. The results showed some decline in blood pressure in every case, with an average drop of 17% in the mean blood pressure. Wilkins and associates [4] confirmed the findings of Freis and co-workers that chlorothiazide is a potent hypotensive agent both alone and in combination with other drugs.

The use of chlorothiazide at the Lahey Clinic was begun in November, 1957. Since then we have attempted (1) to evaluate its effects as a hypotensive agent, (2) to compare its effectiveness with and without the simultaneous use of ganglion blocking agents or previous splanchnicectomy, (3) to determine its effect on potassium excretion as measured by the serum potassium levels and electrocardiographic changes, and (4) to determine the indications for and contraindications to its use in the treatment of hypertensive patients.

Wilkins and associates,[4] in their original paper on chlorothiazide as a hypotensive drug, pointed out the potential danger of the loss of electrolytes of sodium and potassium. Hyponatremia may cause weakness, lassitude, and muscle cramps, but the loss of potassium presents a real danger in patients taking digitalis. The potentiation of digitalis effect in patients with hypokalemia may cause cardiac standstill. Wilkins [4A] postulated this possibility as a cause of death in six digitalized patients early in his experience with chlorothiazide.

A combination of diuresis from mercurial diuretics and hypokalemia from chlorothiazide and digitalis could be fatal. A long-sustained, unrecognized hypokalemia resulting from chlorothiazide could cause a specific tubular type of nephritis. It was for the purpose of preventing such potential complications that we undertook to study our patients with regard to the effect of chlorothiazide on the potassium level of the blood serum.

Methods

A knowledge of the variables that will be encountered is important in studying any hypotensive agent. One example is the discrepancies of blood pressure readings in the home, office, or hospital as taken by the patient, physician, or nurse respectively. The efficacy of any antihypertensive therapy is dependent on an adequate evaluation of the severity of the disease before treatment is initiated.

A series of 65 patients with hypertension without edema was used as the basis for our study. Twenty-one of these patients had grade 3 or 4 hypertension as determined by the Keith-Wagener-Barker method for the classification of ocular fundal changes. Additional data regarding cerebral, cardiac, and renal function were included in the evaluation of the hypertensive status. In 23 cases, ganglion blocking agents had been given prior to and during the initiation of chlorothiazide therapy; splanchnicectomy had been performed previously on seven

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patients. Thirty-three patients were hospitalized for four to seven days before chlorothiazide therapy was begun so that basal blood pressure readings could be determined. All patients who were started on chlorothiazide therapy in the clinic had had follow-up studies for at least three months to as long as several years, and the basal blood pressures were determined by averaging the previous readings. These were compared with the average blood pressure reading over the ensuing period of treatment, which ranged from two to seven months. While therapy with the previously given hypotensive drugs was continued, 0.25 Gm. of chlorothiazide was given twice daily in most cases—the maximum daily dose being 1.0 Gm. and the minimum daily dose 0.25 Gm.

Data from Twenty-eight Patients in Whom Serum Potassium Levels Decreased to 3.5 mEq. per Liter or Below

		Serum Potassium Level, mEq. per Liter		Interval to Lowest Level, Days	Chlorothiazide Dosage		Potassium Chloride Dosage, Gm./Day	Interval to Return to Normal, Days	
Case No.	Grade of Hypertension	Treatment Begun	Lowest Level		Gm.	Times Daily			Remarks on Serum Potassium Level
2	2		1.7		0.25	2	1.2		
5	2		3.5		0.25	2	none		
7	2		2.8		0.5	2	2.0		
12	4		3.5		0.25	1	none		
18	2		3.5	9	0.25	2	none	6	
22	2		3.5	27	0.25	2	none	42	
23	2	3.8	3.3	10	0.25	2	none	39	
28	2	4.2	3.4	56	0.25	2	1.2		
30	2		3.3	90	0.25	2	2.0	90	
32	4	3.5	2.9	4	0.25	2	none	70	
34	3	4.6	3.1	8	0.25	2	none*	28	
35	2		3.5	27	0.25	3	none		
37	2	4.9	2.8	42	0.25	2	2.0		Below 3.5 mEq./liter at last visit
41	3	4.6	3.1	7	0.25	2	3.0		Last seen 66 days later; below 3.5 mEq./liter
44	4 (splanchnicectomy)	3.9	3.5	13	0.25	3	3.0	9	
45	3, 4	4.2	2.8	48	0.25	4	3.0	90	
46	1		3.4	3	0.25	2	none*		
47	2 (splanchnicectomy)	4.8	3.2	42	0.25	3	2.0		Increased to 4.9 mEq./liter when last seen
48	3	3.7	1.8	60	0.25	2	3.0		1.8 mEq./liter when last seen: chlorothiazide therapy stopped for 2 days; potassium chloride increased to 3 Gm. daily; chlorothiazide decreased to 0.25 Gm. daily; electrocardiogram showed hypokalemia
49	2, 3	5.1	2.3	40	0.25	2	none*	150	
51	3, 4	4.2	3.0	100	0.25	2	3.0		Serum potassium level still low: blood pressure did not respond; sympathectomy done
52	2	4.8	2.4	42	0.25	2	none*	60	
53	2 (splanchnicectomy)		3.0	33	0.25	2	none*	36	
54	3, 4	4.5	3.3	4	0.25	2	none	50	
55	1		3.3		0.25	every other day	none		Low serum potassium level on doses of only 0.25 mg. every other day
56	2		3.1	90	0.25	2	none*	60	Potassium chloride withdrawn because of gastric irritation
63	4		1.8	14	0.50	2	none*	14	Symptoms of weakness: prolonged Q-T interval (see text)
65	1 (splanchnicectomy)	4.2*	2.9	70	0.25	2	0.25		70 days later, below 3.5 mEq./liter; chlorothiazide therapy stopped for 1 wk., then one-half of dose given; potassium chloride increased to 3 Gm. daily; serum potassium level still only 3.3 mEq./liter 6 wk. later

* Potassium chloride therapy started after low result of serum potassium determination (in our laboratory, standard deviation for serum potassium level is 1 mEq. per liter, with a normal range of 3.3 to 5.8 mEq. per liter).

Serum potassium determinations were obtained twice a week for the first two weeks and then twice a month or at monthly intervals on return visits to the clinic. Serum sodium values were determined in 47 patients, and all patients were given a 4-Gm. sodium diet during the study.

Results

A decrease in the mean blood pressure of over 10% was noted in 52 patients (80%). Only 2 of the 21 patients with grades 3 and 4 hypertension showed less than a 10% drop in the mean blood pressure. Of the 23 patients receiving ganglionic blocking agents, three failed to show a significant drop in blood pressure.

One of these three (case 63) was a 36-year-old man with a one-year history of malignant hypertension. He had received 0.5 Gm. of chlorothiazide twice daily for three weeks in another hospital before entering the New England Deaconess Hospital, Boston; pentolinium (Ansolysen), 20 mg. four times daily, had also been given. Two episodes of transient aphasia had occurred in the previous two weeks. On admission, the blood pressure was still 250/150 mm. Hg. Chlorothiazide therapy was discontinued because of hypokalemia with a serum potassium level of 1.8 mEq. per liter. At this point he suffered a cerebral hemorrhage with hemiplegia. During the next three weeks of hospitalization, the blood pressure was controlled with hexamethonium. He was discharged on a regimen of mecamylamine (Inversine) hydrochloride and reserpine (Serpasil).

Another patient (case 51), a 32-year-old man with a 13-year history of hypertension, was admitted to the hospital with grade 3 to 4 hypertension. He had been receiving chlorothiazide (0.25 Gm. twice daily) for 15 weeks, along with mecamylamine, 2.5 mg. twice daily, and reserpine, 0.25 mg. twice daily. Because he was emotionally unstable, tense, and nervous as a result of hypertensive encephalopathy, he could not be treated on an outpatient basis; moreover, the blood pressure showed no response to chlorothiazide and the ganglionic blocking agents even in the hospital. He was therefore subjected to bilateral splanchnicectomy. After this, not only was a dramatic response seen in the blood pressure but also the retinal hemorrhages cleared and emotional lability improved.

The third patient (case 53) who failed to show a response to chlorothiazide was a 54-year-old woman with a 14-year history of hypertension. She was receiving mecamylamine (2.5 mg. twice daily) and Rauwolfia for grade 2 hypertension. No response in blood pressure was noted after chlorothiazide was added to this regimen. It may be of significance to add that in all three of the above patients who failed to show a response to chlorothiazide a fall in serum potassium levels to 2.0 and 3.0 mEq. per liter occurred despite the coadministration of 2 to 3 Gm. of potassium chloride daily. Thus, these three patients demonstrated a diminished ability to conserve potassium while chlorothiazide therapy was given.

Of the seven patients who had previously undergone splanchnicectomy, a pronounced drop in blood pressure was noted in all cases—the average drop being 52/39 mm. Hg or a 27% fall in the mean blood pressure. Three of these showed a marked hypotension, and the dosage of chlorothiazide was limited to 0.125 Gm. given twice daily. Two patients who had had splanchnicectomy were given ganglionic blocking agents; both were able to discontinue therapy with these agents when chlorothiazide was administered.

Therapy with ganglionic blocking agents was discontinued in 12 patients, and in an additional 6 the dosage could be reduced by two-thirds or one-half. Thus, the usual dosage had to be continued in only 5 of the 23 patients. Although a drop in blood pressure was noted during chlorothiazide therapy in 77% of the patients with grades 1 and 2 hypertension, it was usually less than that demonstrated in the patients with grades 3 and 4 hypertension. Of the 13 patients who showed less than a 10% fall in the mean blood pressure, the hypertension was classified as grades 1 and 2 in 10. Blood pressures returned to normal levels in 28 of the 65 patients; in 6 additional patients the diastolic pressure re-

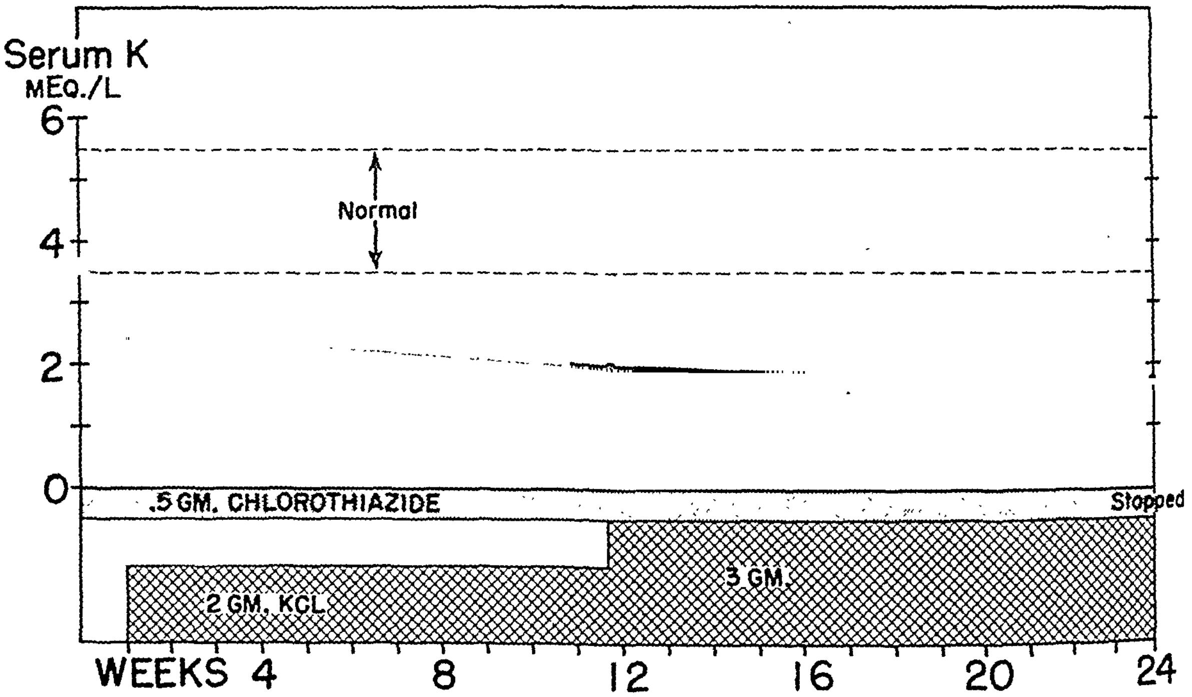

Fig. 1 (case 48).—Inability to conserve potassium. Serum potassium level continued to drop to level of 1.8 mEq. per liter despite administration of 3 Gm. of potassium chloride daily.

turned to a normal level. Thus, approximately one-half of the patients had normal blood pressure readings after chlorothiazide was added to the program of therapy.

The striking finding in the group of 65 patients studied was the fact that 28 patients (43%) showed a drop in serum potassium levels to 3.5 mEq. per liter or below, as demonstrated in the table. Of these 28 patients, the average fall in serum potassium level was 1.5 mEq. per liter, despite the fact that 12 patients had received 2 or 3 Gm. of potassium chloride daily from the time chlorothiazide therapy was started. One patient (case 55) received only 0.25 Gm. of chlorothiazide every other day, and the serum potassium level fell to 3.3 mEq. per liter. In another patient (fig. 1, case 48), who received 0.25 Gm. twice daily, the serum potassium level fell to 1.8 mEq. per liter and the electrocardiogram showed definite hypokalemic changes despite the concurrent administration of 3 Gm. of potassium chloride daily. However, the hypertension changed from grade 3 to grade 1 six months after chlorothiazide therapy was begun, and the patient was able to stop taking mecamylamine four months after administration of chlorothiazide was initiated. One of the patients (case 63) mentioned above as having no fall in blood pressure while receiving 0.5 Gm. of chlorothiazide twice daily for three weeks, along with pentolinium and hydralazine (Apresoline) for malignant hypertension, exhibited a decrease in serum potassium level to 1.8 mEq. per liter with symptoms of nausea and weakness. The electrocardiogram demonstrated pronounced hypokalemia, with the Q-T interval prolonged to 67% of the R-R interval. He had not received potassium chloride, and the blood pressure had remained at 250/150 mm. Hg. As evidence of pronounced potassium depletion, 40 mEq. per liter of potassium chloride was administered intravenously each day for one week before the serum potassium level reached a level of 3.7 mEq. per liter. This same patient also exhibited signs of hypochloremic alkalosis, with an initial carbon dioxide–combining power of 34 mEq. per liter and chloride level of 92 mEq. per liter. The aldosterone assay gave normal results.

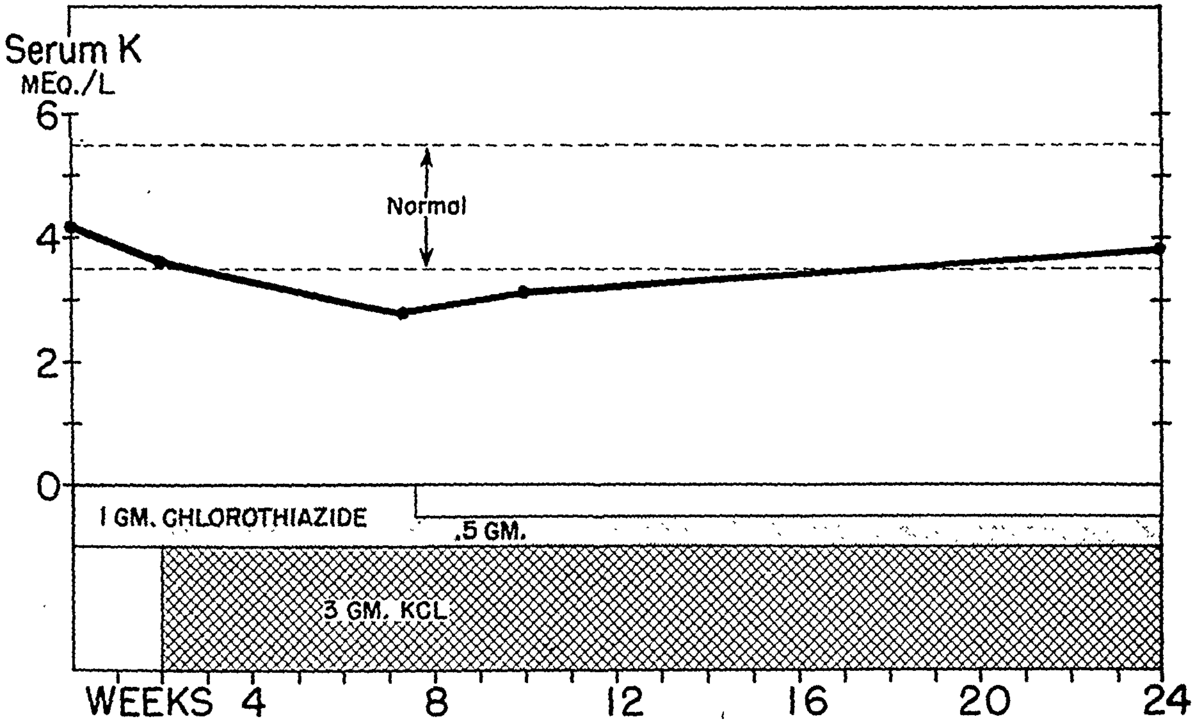

Fig. 2 (case 45).—Graph illustrating necessity of lowering dosage of chlorothiazide when potassium chloride has been added and serum potassium level continues to fall.

Three patients could not tolerate potassium chloride because of gastric irritation. It was necessary to stop chlorothiazide therapy because of low potassium levels in only two instances (case 48 [fig. 1] and case 63).

The fall in serum potassium level will usually be apparent after seven days. However, in one patient (case 54) the serum potassium level dropped from 4.5 mEq. to 3.3 mEq. per liter on the fourth day after chlorothiazide therapy was instituted.

Frequently, the lowest serum potassium level was not reached until four to six weeks after chlorothiazide therapy was started, as shown in figures 2, 3, and 4. The administration of 2 to 3 Gm. of potassium chloride daily usually brought the serum potassium level back to normal. There were many exceptions to this, however, and in a few instances the serum potassium value continued to decline but would no doubt have fallen even more had potassium chloride therapy been withheld.

Comment

Our experience at the Lahey Clinic has shown that chlorothiazide is an effective agent in the treatment of hypertension. Because it augments blood pressure response to other hypotensive agents, smaller and less frequent doses of the latter are needed. Thus, one of its greatest advantages is in the treatment of patients with grades 3 and 4 hypertension. In such cases the dose of ganglionic blocking agents may be either cut in half or entirely eliminated, thereby reducing the side-effects to a tolerable level. In addition to decreasing the side-effects, it decreases the pronounced fluctuation in blood pressure that accompanies the administration of various ganglionic blocking agents. We concluded that chlorothiazide not only potentiates the effect of other hypotensive agents but also appears to have a decided antihypertensive influence in its own right.

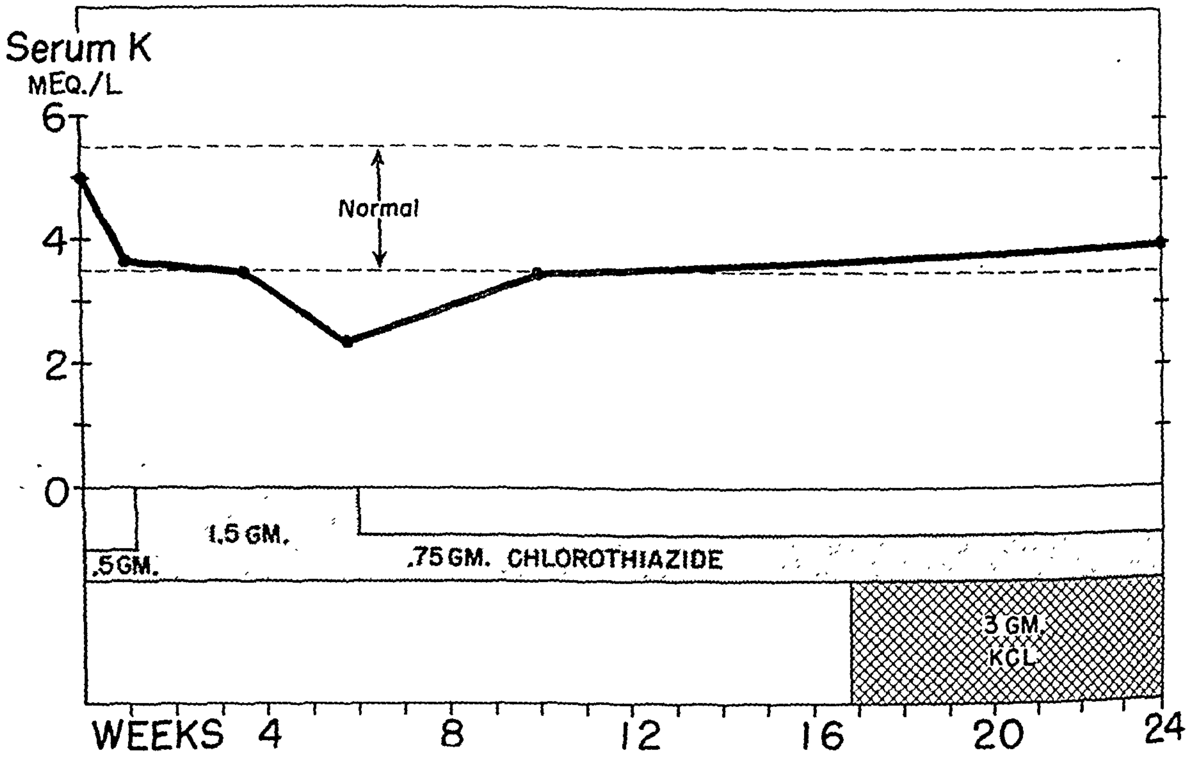

Fig. 3 (case 49).—Return of serum potassium level to normal limits with decreased dosage of chlorothiazide and addition of 3 Gm. of potassium chloride.

Chlorothiazide administered orally in doses of 500 mg. each day can produce a significant change in the serum potassium level. In our series a drop to 3.5 mEq. per liter or below was noted in 43% of the patients. This is substantially greater than the decrease reported earlier by Wilkins and associates.[4] In their series, only 3 of 17 patients showed a drop in serum potassium level below 3.7 mEq. per liter. Moreover, in our series the average daily dose was 500 mg., whereas they used 750 mg.

In only 6 of the 28 patients in whom the serum potassium level dropped to below 3.5 mEq. per liter did it return to normal without the help of either potassium chloride supplement or reduction of the dosage of chlorothiazide. The drop occurred in many instances despite the concurrent administration of 2 to 3 Gm. of potassium chloride daily.

It may be seen in the table, however, that there were many exceptions; in 10 cases the potassium level remained below 3.5 mEq. per liter for a much longer time. The long-term use of drugs which may cause potassium depletion must be carefully considered in these patients who are potential potassium wasters.

Considerable evidence has indicated that potassium deficiency may cause significant alterations in renal structure and function.[5] Dietary deficiencies of potassium in rats and mice produce enlargement of the kidneys and striking changes in the tubular structure.[6] The increase in size begins within a few days, and the kidneys often become twice normal size in two weeks. The most striking changes occur in the collecting tubules where swelling, hyperplasia, and granulation [7] are noted. Restoration of potassium to the diet has resulted in virtually complete healing of the characteristic lesion.[8] However, other observers have noted interstitial scarring, hyalinized glomeruli, and dilated tubules several weeks or months after correction of a deficiency which lasted for six to eight weeks.[6]

It is now well recognized that renal lesions may accompany potassium deficiency in man.[5] Such changes have been described in various diseases associated with potassium deficiency; depletion produced by diarrhea in ulcerative colitis or bacillary dysentery and chronic small intestinal fistulas; adrenal disease such as adrenal cortical hyperfunction (Cushing's syndrome), primary aldosteronism, and the condition after cortisone treatment; and, finally, renal diseases with potassium wasting, such as renal tubular acidosis and macrocytic anemia (Fanconi's syndrome), subacute glomerulonephritis, and chronic pyelonephritis.

The minimum duration and severity of the potassium depletion required to produce these changes in man are not known, but the condition has usually been present for many months before such changes occur. In many of our patients, the serum potassium level was below 3.5 mEq. per liter on return visits over a period of several months. Because this occurred in some instances despite added potassium, it would seem advisable to reevaluate renal function in these patients who have proved to be potassium wasters. Thus far we found no alteration in renal function.

Postmortem observation of changes in renal structure in patients who had received chlorothiazide with prolonged potassium depletion will provide the final answer. We know of no such reports, nor have we seen a patient who has had digitalis poisoning potentiated by hypokalemia resulting from chlorothiazide therapy. The danger of such an occurrence must be borne in mind, however.

Summary

The effect of chlorothiazide was studied in a series of 65 hypertensive patients. A definite hypotensive effect was observed in 80% of the patients. This effect was more pronounced in patients with severe hypertension and in those receiving ganglionic blocking agents; it was most pronounced in patients who had previously undergone splanchnicectomy.

Of the 23 patients who had formerly required ganglionic blocking agents, 12 were able to discontinue that therapy and an additional 6 were able to reduce the dosage to one-half or less when chlorothiazide was administered.

Twenty-eight patients (43%) showed a drop in serum potassium level to 3.5 mEq. per liter or below. This occurred in 12 patients despite the concurrent administration of 2 to 3 Gm. of potassium chloride daily. It is now well recognized that renal lesions may accompany potassium deficiency in man. We know no way of predicting which patients will show potassium waste, since in our series depletion has occurred with or without impaired renal function.

The symptoms of potassium deficiency may be minimal and their onset insidious. It would seem that periodic determinations of the serum potassium level are necessary in any patient who is receiving chlorothiazide treatment for hypertension on a long-term basis. Such patients should be instructed

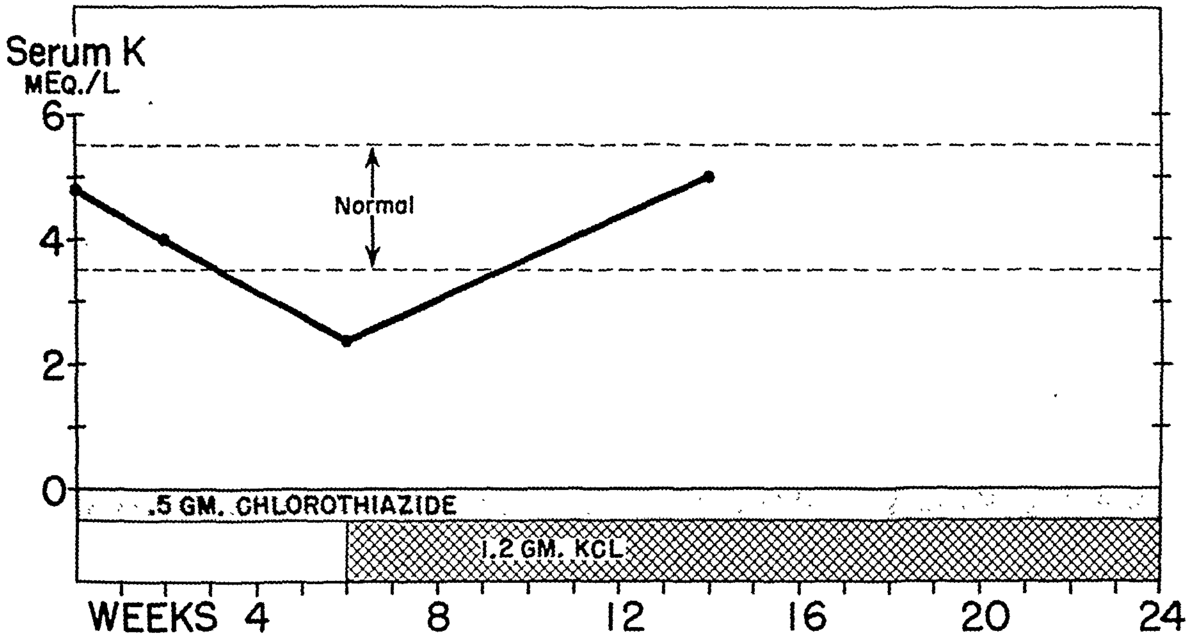

Fig. 4 (case 52).—Usual response of serum potassium level when potassium chloride has been added.

to interrupt the use of this drug when conditions associated with diarrhea or vomiting occur. When these conditions are present, the additional potassium losses that occur could result in severe potassium depletion.

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CLINICAL NOTES

CORONARY EMBOLUS

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The occurrence of coronary embolus in a patient with rheumatic heart disease is an unusual complication. No means of differentiating it from acute coronary thrombosis exists.[1] One should be suspicious of acute coronary embolus if the clinical picture of acute coronary thrombosis occurs in a young patient in whom advanced coronary disease is unlikely. This suspicion should be increased, especially, if the patient has not had angina pectoris and if auricular fibrillation and mitral stenosis are present.

The most frequent cause of coronary artery embolus is subacute bacterial endocarditis. Occlusion is more common in the left artery than in the right. Two-thirds of all patients with coronary embolus due to bacterial endocarditis die suddenly; the remaining third have a longer course which simulates acute myocardial infarction. When embolism is due to disease other than bacterial endocarditis, the outcome is always fatal, according to published reports.[2]

To establish that death is due to coronary embolism, postmortem study should reveal an occluding mass in a major branch of the coronary system, as well as the site of origin of the embolus and normal arterial intima at the area of occlusion.[2] Sometimes a coronary embolus may arise from a calcified valve in a patient with healed bacterial endocarditis.[3]

A case of chronic rheumatic heart disease, with multiple emboli to the lower extremities, kidneys, and lungs and fatal embolism to the heart, is presented here.

Report of a Case

A 42-year-old woman with chronic rheumatic heart disease of many years' duration was seen because of pain and numbness in the right leg, with sudden onset one-half hour earlier. No pulsations were present in the right lower extremity, and oscillometric readings were absent. The onset of rheumatic fever occurred at the age of 10 years, with recurrence three times between the ages of 10 and 12. At the age of 21 years, the patient had scarlet fever, complicated by pneumonia, for which she was bedridden eight weeks. On recovery, she was placed on therapy with digitalis, which she had taken continuously since that time. The patient was married and had two children. Since the age of 28, she had noted a progressive loss of strength, associated with intermittent swelling of the legs and ankles.

Examination on admission to Hackensack (N. J.) Hospital showed a middle-aged, slender woman appearing chronically ill and weighing 110 lb. (49.9 kg.). Her fibrillation rate was about 90 per minute, as confirmed by electrocardiogram, which also showed digitalis effect. The heart was enlarged to the left anterior axillary line in the sixth intercostal space. The first heart sound was accented and snapping in quality. An opening snap

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was heard. The second pulmonary sound was accentuated and split. Along the left parasternal border, a blowing diastolic murmur was heard. A grade-3 systolic murmur was present at the apex and transmitted throughout the precordium. A grade-2 presystolic murmur was also present at the apex, accompanied by a thrill.

The surgical consultant concurred in the diagnosis of embolus to the right femoral artery, and embolectomy was performed within five hours. Postoperatively the patient did well, but a postoperative electrocardiogram showed evidence of anteroseptal myocardial infarction. She was placed on anticoagulant therapy (heparin and bishydroxycoumarin) and had an uneventful convalescence. She was discharged in good condition after six weeks, with all pulsations in the right lower extremity of good quality.

About eight hours after leaving the hospital she was seen again because of numbness and tingling in her left lower extremity. These complaints had developed shortly before her discharge from the hospital, but since they were mild she did not say anything about them for fear she would not be released. No pulsations were palpable in the left lower extremity, and no oscillometric readings could be obtained. She was readmitted, but three more hours elapsed before operation, when an embolus to the profunda branch of the left femoral artery was found. An embolectomy was performed, but the dorsalis pedis pulsation still was not palpable. Because the patient's condition was deteriorating, the operation was terminated. Postoperatively, the color of the left lower extremity was good but absence of pulsations persisted and the patient complained of pain, numbness, and coolness of the leg. The pain at times was excruciating and was controlled only with narcotics. Nerve blocks were performed but did not control the pain.

After several weeks, a plastic bypass graft was inserted around the obstruction and a sympathectomy was performed simultaneously. For one day after the operation, the leg felt warmer and there was less pain. However, the pain recurred and again could be controlled only with narcotics.

She was transferred to St. Vincent's Hospital, New York City, on May 11, 1958. Physical findings were as previously reported except for a loss of weight from 110 lb. to 78 lb. (35.4 kg.). The left lower extremity was swollen and atrophic and felt cool; no pulsations were present. The right lower extremity felt warm, and strong pulses were felt in the femoral, popliteal, and dorsalis pedis arteries.

An aortogram showed obstruction of the left external iliac, common femoral, and proximal half of the superficial femoral arteries. An electrocardiogram showed fibrillation (auricular) at a rate of 100 per minute. The urine was negative for sugar and albumin but contained many white blood cells and bacteria per high-power field. The blood cell count was within normal limits. X-ray of the chest showed cardiac enlargement.

She was seen by the cardiopulmonary staff and the combined medical-surgical cardiac team, who advised against operation because of her poor general condition. Shortly afterward, she developed pneumonia of the lower lobe of the left lung, which responded to penicillin treatment. On recovery, she was seen by the medical consultant, who felt that mitral commissurotomy might help. She was discharged for convalescence at home and was to return in one month for cardiac surgery.

Two days after returning home, she was awakened by severe pain in the right flank. She was readmitted to St. Vincent's Hospital. The pain persisted for several days, but results of urinalysis were negative for red blood cells. The temperature reached a peak of 102 F (38.9 C). Five days after admission, she developed severe pain in the left flank and results of urinalysis were again negative for red blood cells. Her complaints gradually subsided, and she was discharged for convalescence at home.

The patient entered St. Vincent's Hospital for the third time on Aug. 20. Five days after her admission, a temperature of 101 F (38.3 C) was noted, associated with a loose, productive cough. Rhonchi were heard in both lung bases. After administration of penicillin, the temperature returned to normal but then rose again. Blood culture showed no growth. Pain appeared in the lower right part of the chest anteriorly, and a friction rub and rales were heard.

On Sept. 10, slight induration along the lesser saphenous vein on the left was observed, and two days later severe pain in the anterior right part of the chest occurred again. On Sept. 13, ligation of the left common femoral vein was performed with the patient under local anesthesia. The patient tolerated the procedure well, and the postoperative course was uneventful until Sept. 20, when severe pain in the anterior part of the chest, radiating to both shoulders and arms, developed. The blood pressure was 90/72 mm. Hg, pulse rate 128 per minute, thready and irregular, and respiration rate 32 per minute. The lips and nails were cyanotic. The patient had dyspnea and orthopnea and was apprehensive. The heart sounds were of good quality. Coarse rales were heard throughout the chest. An electrocardiogram showed anterior wall infarction. The patient was placed in an oxygen tent. She died about 16 hours after onset of the acute chest pain.

At autopsy, the lungs were congested and edematous, with infarction of the lower lobes of the right and left lungs. The liver and spleen were moderately congested. Both kidneys showed congestion and infarction. There was congestion also of the stomach and small and large intestines. Petechial hemorrhages were present in the stomach. The aorta showed minimal focal atherosclerosis.

The heart, weighing 450 Gm., was moderately enlarged and dilated. The left auricle contained a mural thrombus which extended to and completely filled the auricular appendage. The mitral valve showed extreme stenosis, and the mitral opening was fish-mouthed in appearance and would not admit a finger. The mitral cusps were thickened and fused. The left ventricular wall measured 1 cm. in thickness. The coronary ostia were patent, and the arteries were thin and pliable, with a pale, smooth intimal surface. One centimeter from the left coronary ostium, in the left anterior descending branch, the lumen was completely occluded by pinkish-gray, granular, friable material similar to that noted on the endocardial surface of the left auricle.

Conclusions

A case of coronary embolus occurred secondary to chronic rheumatic heart disease in a 42-year-old woman. Suspicion of coronary embolism should be aroused when the symptoms of acute coronary thrombosis occur in a young patient, especially when there is no history of angina pectoris and when auricular fibrillation and mitral stenosis are also present.

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CORONARY EMBOLISM WITH MYOCARDIAL INFARCTION—COMPLICATION OF VERRUCOUS ENDOCARDITIS

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Coronary embolism, as a cause for myocardial infarction, has probably been diagnosed clinically only three or four times.[1] Small coronary emboli are usually of little clinical significance and are not infrequently seen at autopsy in cases of bacterial endocarditis [2] and in some forms of verrucous endocarditis (verrucal endocardiosis).[3] Emboli large enough to produce gross myocardial damage have been reported convincingly in only about 50 cases.[1] The literature on this subject has been reviewed several times in recent years.[4] The emboli reported have almost always been blood clots which have arisen either from lesions within the coronary arteries, aorta, or endocardium or from the lower extremities by way of a patent foramen ovale. There are only two reports of nonthrombotic emboli. These included a calcified nodule arising from the aortic valve [4b] and a caseous plug arising from the lungs in a case of pulmonary tuberculosis.[5] To our knowledge, there are only two cases in the literature with electrocardiographic evidence of myocardial infarction.[6]

The case reported here is of interest since a new type of embolic material was identified, namely, a verruca dislodged from the site of verrucous endocarditis on a heart valve. Electrocardiographic data are also presented. The infarction was diagnosed clinically.

Report of a Case

Clinical History.—The patient was a 44-year-old woman who was well until October, 1955, at which time she developed thrombophlebitis of the left leg. This was followed in six weeks by an attack of acute, severe pain in the lower part of the abdomen. An exploratory laparotomy performed at another hospital revealed a large papillary adenocarcinoma of the left ovary, for which the patient had a bilateral salpingo-oophorectomy. Despite a postoperative reactivation of the thrombophlebitis and one episode of pulmonary embolization, she gradually improved. After discharge, she was given a series of 24 x-ray treatments to the abdomen over a period of three months. Thereafter she did well until August, 1956, when she again developed thrombophlebitis of the left leg, followed by progressive enlargement of the abdomen with loss of appetite, constipation, and generalized abdominal pain. She was admitted to the Lenox (N. Y.) Hill Hospital on Sept. 12, 1956, and two days later a laparotomy was performed by Dr. John Vieta. The findings included several liters of bloody ascitic fluid, generalized carcinomatosis, and obstruction to the transverse

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colon from tumor nodules. The obstructed section of the transverse colon was resected and closed with an end-to-end anastomosis. The pathologist's report indicated that the tumor was a papillary adenocarcinoma. Prior to discharge, she was treated with one intraperitoneal dose of radioactive colloidal gold and three intravenous doses of 2 mg. of triethylene melamine. The patient was discharged on Oct. 12, 1956. During the next two weeks, she required several transfusions at home.

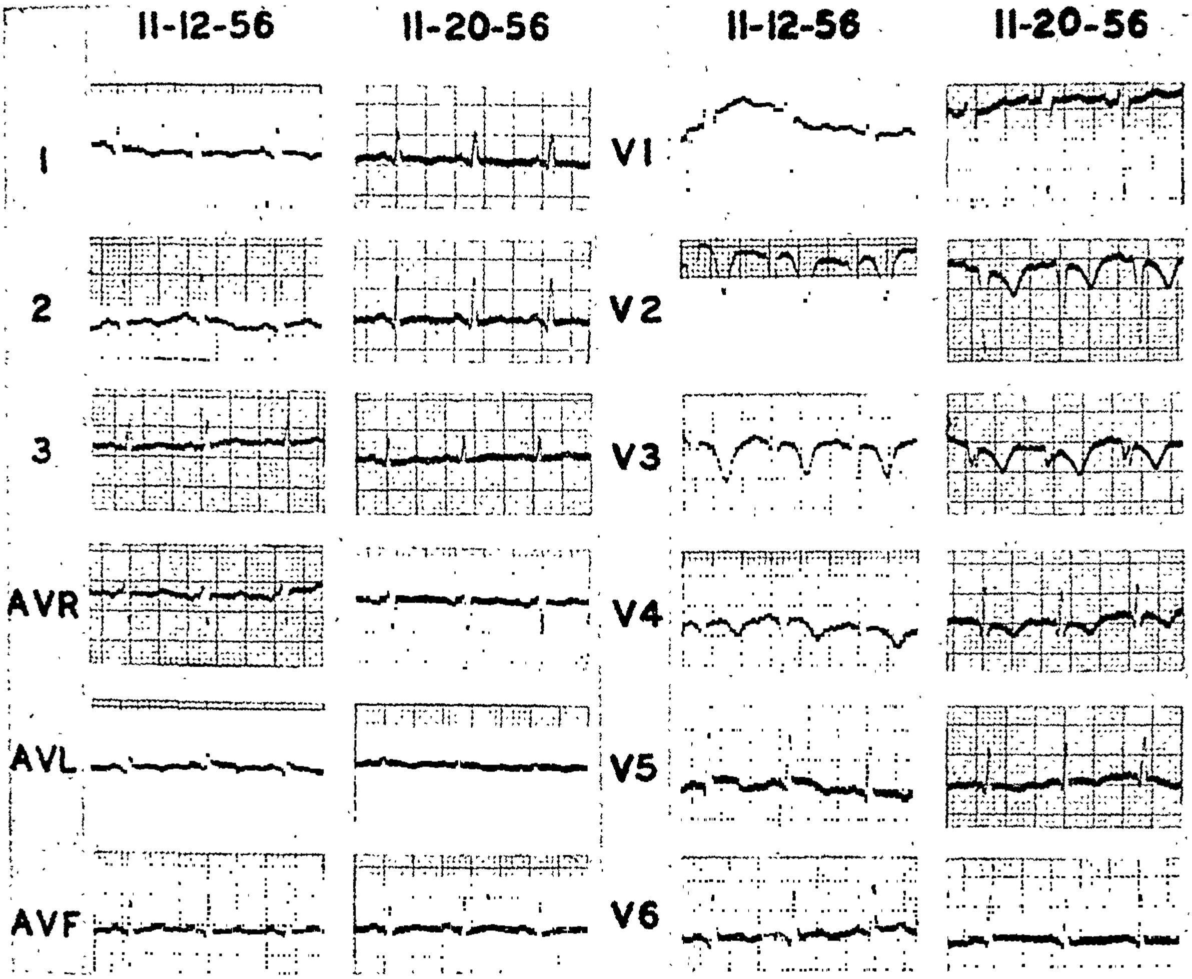

Fig. 1.—Electrocardiograms taken 14 days (11-12-56) and 20 days (11-20-56) after clinical episode of chest pain.

On Oct. 29, she had a severe bout of nausea and vomiting after which she had a crushing pain in the anterior part of the chest, radiating to both arms and to the mid-back. The patient was in a cold sweat during the attack, which lasted for several hours. She required morphine and meperidine (Demerol) throughout the night. During the subsequent 11 days prior to admission to the Norwalk (Conn.) Hospital, she experienced extreme weakness and had a persistent fever and tachycardia and became forgetful, drowsy, and apathetic.

On admission to the Norwalk Hospital, the patient was in no acute distress but was confused mentally and disoriented as to her surroundings. Complete physical examination was negative, except for evidence of marked pallor, a pulse rate of 110 per minute, and the presence of two long abdominal incisional scars. The impression on admission was that the patient either had metastatic brain damage or cerebral emboli, possibly arising from a damaged myocardium.

On admission, the hemoglobin level was 10.4 Gm.%, red blood cell count 3,120,000 per cubic millimeter, and white blood cell count 2,750 per cubic millimeter with 68% adult polymorphonuclear cells, 14% stab cells, 16% lymphocytes, 1% monocytes, and 1% basophils. Urinalysis revealed a specific gravity of 1.026, pH 7, 1+ albumin, a few white blood cells, and no sugar. The blood urea nitrogen level was 11 mg.%, chloride level 97 mEq. per liter, and Venereal Disease Research Laboratory test result negative. An electrocardiogram taken on Nov. 12 showed a pattern interpreted as a recent anterior wall myocardial infarction. Repeated on Nov. 20, the tracing was generally the same, except for a diminution in the depth of the T waves (fig. 1).

Two days after admission, a pericardial friction rub was heard over the left precordial area. Despite tube feedings, intravenous administration of fluids, penicillin, and digitoxin, and other forms of supportive treatment, the patient progressed into a state of stupor, congestive heart failure, and shock and finally died 24 days after admission.

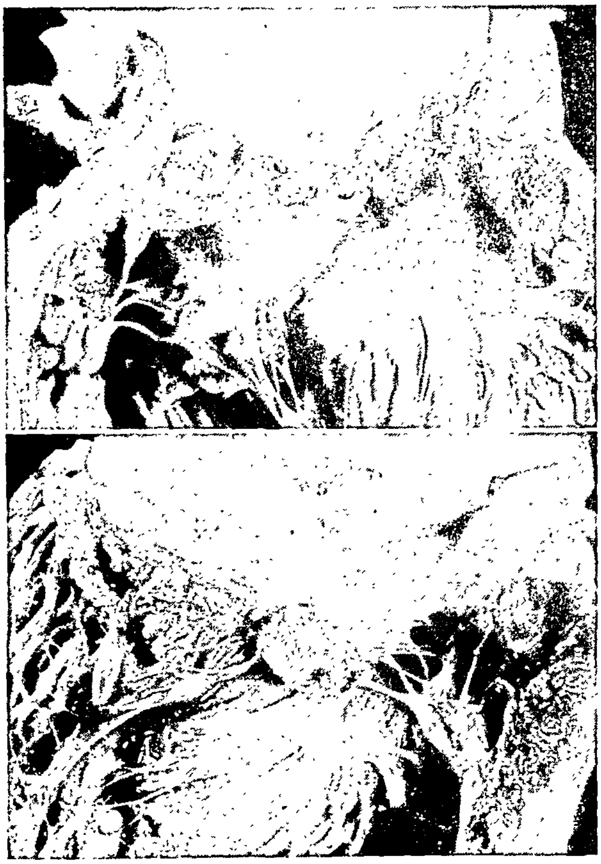

Fig. 2.—*Top,* aortic valve demonstrating many verrucous excrescences on three valve cusps. *Bottom,* mitral valve demonstrating large verrucous masses on both cusps.

Autopsy Findings.—Autopsy was performed by George W. Changus, M.D. The body was well developed but slightly undernourished. There were well-healed abdominal scars and brown pigmentation of much of the abdominal skin. Pitting edema (1+ to 2+) was present in both legs. In the peritoneal cavity there were many dense fibrous adhesions, as well as many tumor nodules confined to the underside of the diaphragm. There was one 5-cm. tumor mass in the left side of the pelvis. The heart weighed 240 Gm. On both mitral and aortic valve cusps there were slightly firm, granular, pale pink masses of friable material measuring from 5 to 20 mm. in greatest diameter (fig. 2). These masses were somewhat adherent to the valve cusps but were not associated with destruction or fibrosis of the leaflets. There were no adhesions of the commissures, and the chordae tendineae were thin and delicate. One of the aortic valve vegetations partly occluded the left coronary ostium. A mass of similar material was impacted, though not firmly adherent, in the left main coronary artery 1 cm. proximal to its bifurcation (fig. 3). There was extensive yellow-brown infarction of the myocardium of the anterior wall of the interventricular septum. The left pulmonary artery contained a thrombus, but there was no infarct of the lung. The spleen weighed 340 Gm. and was about half replaced by dark red infarcts measuring up to 5 cm. in diameter. The kidneys weighed 100 Gm. each and were about three-quarters replaced by infarcts varying from white to dark red in color. Adherent thrombi were found in the renal arteries and veins. Both iliac veins were occluded by adherent thrombi, partly firm and white and partly red and friable. These thrombi extended up the inferior vena cava to the hepatic veins. The liver weighed 1,650 Gm. and was about 5% replaced by white tumor nodules. The adrenals were slightly atrophic. The brain contained an area of gray-tan softening in the frontoparietal area. The other organs were free of major gross lesions.

Microscopically, a papillary cystadenocarcinom of typical ovarian morphology, with a few psammoma bodies, was identified in sections of live lung, and tissues of the pelvis and diaphragm. The verrucous material on the heart valves had the peculiar refractile, deeply eosinophilic, acellular appearance characteristic of verrucous endocarditis

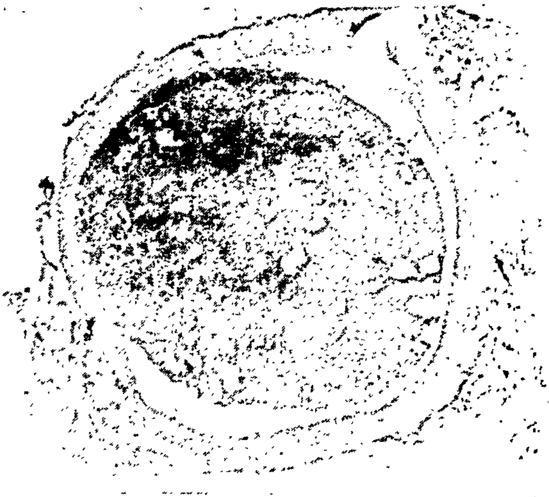

Fig. 3.—Cross section through verrucous embolus *lodge* in left main coronary artery (×10).

It stained the bright blue of collagen with Masson stain (using aniline blue counterstain). The co lagen could readily be distinguished from the re to orange color of the fibrin, which was sometime adherent to it. The verrucous material also had markedly positive reaction to the periodic acid

Schiff test. Where the vegetation arose from the valves there were areas of blending between the valve collagen and the vegetation, and there was an absence of cellular reaction. Emboli having the same tinctorial properties as the verrucae on the heart valves were present in arterial vessels (fig. 4) ranging from arterioles to a major coronary artery and were found in the spleen, pancreas, kidneys, and small intestine as well as the heart. Infarcts varying in age from acute to subacute were present in the heart (fig. 5), spleen, adrenal, kidneys, and brain. True antemortem thrombi were present in the iliac veins and a pulmonary artery. Other positive microscopic findings were slight hyperplasia of the bone marrow and moderate loss of cortical lipid in the adrenals.

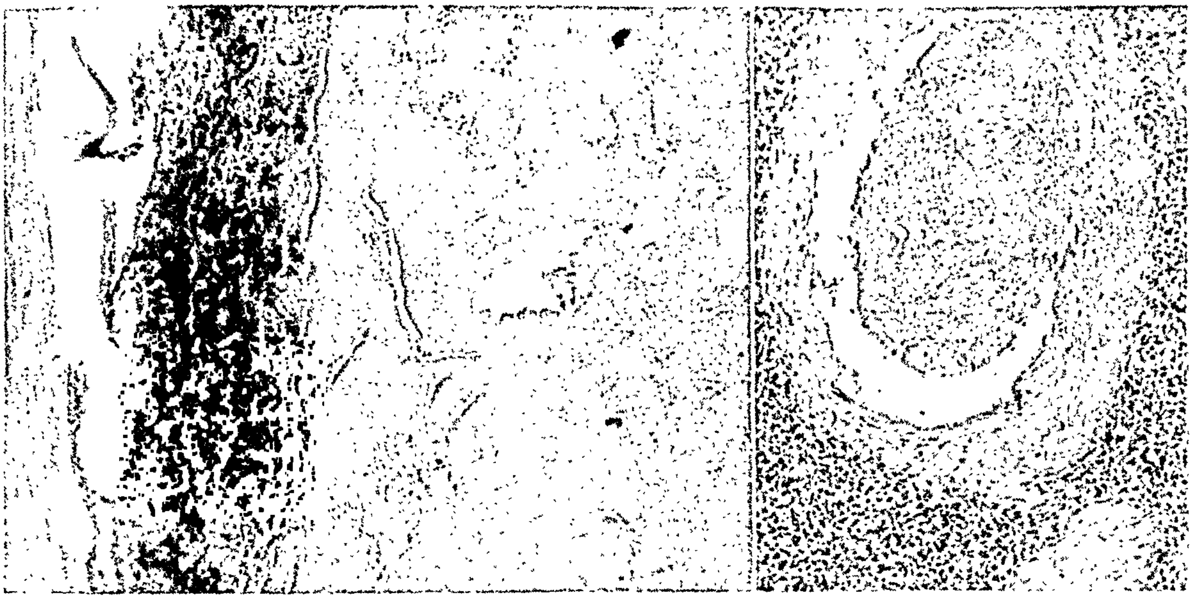

Fig. 4.—*Left*, section of verrucous embolus lying within left main coronary artery (×90). *Right*, verrucous embolus lodged in one of smaller splenic arteries (×50).

Comment

Verrucous endocarditis has been referred to as terminal endocarditis, nonbacterial thrombotic endocarditis, endocarditis simplex, and cachectic endocarditis. Extensive studies by Libman,[7] Gross and Friedberg,[8] and Allen and Sirota [3] have defined this condition as a localized endocardial disease, unrelated to bacterial infection, rheumatic fever, or disseminated lupus erythematosus. Allen and Sirota [3] have suggested that the verrucous excrescences result from degenerative changes in the collagen of the endocardium and heart valves, since the verrucae are argyrophilic and take other stains for collagen. Verrucous endocarditis almost always develops in association with chronic debilitating diseases, such as carcinomatosis, leukemia, tuberculosis, and congestive heart failure. It may, however, occur postoperatively and in other conditions in which a patient's prognosis may be favorable. In the autopsy series reported by Allen and Sirota,[3] 46% of the patients were under 50 years of age. They found that the endocardial lesions were most common in the left side of the heart, especially on the mitral valve. Small verrucae have been recorded as developing from the endothelium of the coronary arteries.

Allen and Sirota have stated, "Occasionally portions of verrucae, particularly of the more friable,

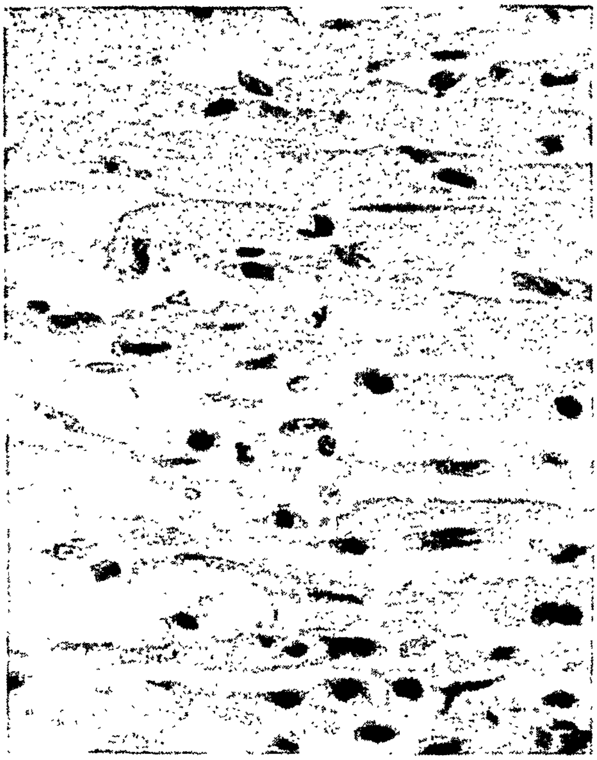

Fig. 5.—Section through myocardium showing recent degeneration of muscle fibers (×240).

exudative type, break off to produce infarcts, and rarely even a fatal encephalomalacia."[3] No cases were specifically cited. The case reported here is the first case, to our knowledge, in which verrucous embolization played such a dominant role clinically. Not only did the patient present a clinical picture and electrocardiographic evidence of a myocardial infarction but there was extensive embolization to the brain, spleen, and kidneys, all of which contributed to the death of this patient.

Summary

Verrucous endocarditis is a fairly common complication of chronic debilitating diseases. In the case described here death was caused by an embolus of verrucous material which arose from an endocardial vegetation, entered a coronary artery, and produced extensive myocardial infarction.

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THROMBOEMBOLIC DISEASE IN ADOLESCENCE

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Pulmonary heart disease resulting from thrombotic occlusion of the small pulmonary arteries due to repeated "silent emboli" has been recognized for some time. Owen and co-workers[1] have reported 12 cases of this rather rare condition in its purest form, uncomplicated by other serious disease, among 8,000 autopsies within a period of 20 years. The ages of the patients ranged from 32 to 72. According to Parker and Smith,[2] the occurrence of embolic phenomena is unusual before the fourth decade.

In a series of 97 cases of fatal pulmonary embolism reported by Fowler and Bollinger,[3] 81% occurred in the group over 40 years of age, the median age group being 60 to 70.

The case presented here appears to involve one of the youngest patients yet reported with massive pulmonary embolism. A similar case in an 18-year-old athlete has been reported by Neuhof and Klein.[4]

Report of a Case

A 15-year-old boy was admitted to Wilson Memorial Hospital on Aug. 6, 1957. About one month before admission, he had experienced increasing weakness and easy fatigability to the extent that he was unable to perform his usual activities. Two days prior to entry, he had a sudden sharp pleuritic pain in the right lower part of the chest, radiating to the back at the level of the eighth intercostal space; it was aggravated by deep breathing and was accompanied by a hacking, nonproductive cough. There was no hemoptysis, weight loss, or dyspnea. There was anorexia, but without bowel or urinary disturbances. The patient had had an appendectomy at the age of 7, measles and mumps, and a tonsillectomy at the age of 6. There was no evidence of heart disease. He was an enthusiastic baseball catcher and had practiced intensively as such for three years prior to admission.

The patient was slender, well-developed, and somewhat apprehensive, although not in acute distress. Physical examination revealed a body temperature of 101.4 F (38.8 C); pulse, 100 beats per minute; and respirations, 25 per minute. The blood pressure was 120/80 mm. Hg. The throat was not injected. Examination of the heart revealed no cardiac enlargement or murmurs. A few coarse crepitant rales were heard at the base of the right lung. No dulness or increased vocal fremitus was noted at that time. The left lung was normal on auscultation and percussion. The abdomen was soft,

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From Charles S. Wilson Memorial Hospital.

and neither the spleen nor the liver were palpable. No calf tenderness and no pretibial or ankle edema was elicited. The peripheral pulses were normal. Examination of the blood revealed a hemoglobin level of 13.6 Gm. per 100 cc. and a white blood cell count of 14,300 per cubic millimeter, with 71% neutrophils (4 band forms) and 1 eosinophil. The urine, with a specific gravity of 1.027, was normal. X-ray of the chest was normal.

The patient was put on chloramphenicol (Chloromycetin) therapy with apparent immediate response. On the third hospital day, his temperature was 99 F (37.2 C), the pulse was 88 beats per minute, and the respirations were 23 per minute. He remained afebrile and continued to do well except for occasional cough and slight chest pain on inspiration. On the 10th hospital day, he suddenly developed increasing dyspnea, followed by extreme restlessness and rapid breathing. The patient was now pale, extremely apprehensive, and in considerable distress, perspiring profusely. The temperature was 101 F (38.3 C) and the pulse, 110 beats per minute and regular. Respirations were very shallow, at the rate of 44 per minute. Harsh breath sounds with a prolonged expiratory phase and coarse crepitant rales were heard in the base of both lungs. Examination of the heart revealed sinus tachycardia (rate, 110 beats per minute) but no murmurs. Blood studies revealed a hemoglobin level of 15.5 Gm. per 100 cc., with a hematocrit value of 47%. The white blood cell count was 17,400 per cubic millimeter, with 81% neutrophils, 5 of which were band forms. The sedimentation rate was 0.3 mm. per minute and the carbon dioxide–combining power, 51 vol.%. Another x-ray examination of the chest was normal. The sodium level was 137 mEq. per liter and the potassium level, 3 mEq.; cephalin flocculation was 2+ in 48 hours. The fasting blood sugar level was 104 mg. per 100 cc.; the serum nonprotein nitrogen level, 31 mg. per 100 cc.; and C-reactive protein precipitation, 1+. No L. E. cells were found in the peripheral blood. Agglutination tests for Brucella, typhoid, and paratyphoid were negative. The heterophil antibody was positive in a dilution of 1 to 28. A lumbar puncture revealed normal spinal fluid dynamics, with 4 lymphocytes per cubic millimeter. The spinal fluid total protein level was 13 mg. per 100 cc.; the sugar level, 94 mg.; and the chloride level, 126 mEq. The tuberculin test (PPD) was negative in 24 to 48 hours.

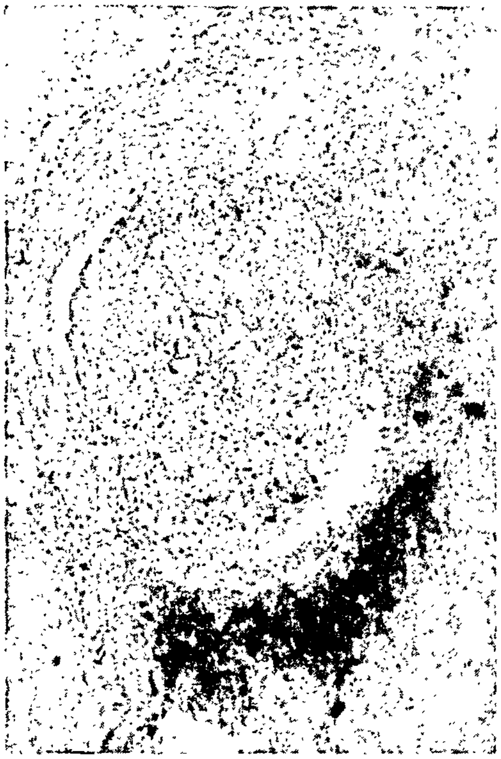
On the next day, the patient complained of joint pains, especially in both knees, the left elbow, and left ankle. An effusion of the left knee joint was noted, as well as swelling of the left elbow and left ankle. All these joints were moderately tender on palpation and motion. A suggestion of a pleural friction rub was detected in the left axillary region. All previous medication was discontinued and antihistaminics were administered, with gradual subsidence of joint symptoms. The patient continued to have a remittent irregular fever, with temperature ranging from 100 to 103.4 F (37.8 to 39.6 C), and frequent unexpected episodes of shallow, rapid respiration, followed by extreme restlessness and mental confusion. Because of suspected personality changes, the patient's increasing apprehension, and frequent episodes of hyperventilation, he was interviewed by a psychiatrist. The patient was found to be intelligent, with a well-integrated personality and without any strong neurotic trends. On the 15th hospital day, there was a sudden onset of sharp pleuritic pain in the left side of the chest, just below the nipple, followed by a persistent productive cough and expectoration of blood-tinged sputum.

The patient was dyspneic, acutely ill, and perspiring profusely. There was definite cyanosis of the fingernails and toenails but no clubbing. A rapid loss of weight had occurred. The temperature was 103 F (39.4 C) and the pulse, 115 beats per minute; respirations were 46 per minute. Examination of the chest revealed diminished breath sounds in the base of the left lung and a pleural friction rub in the lower part of the right lung. The abdomen was soft. Moderate tenderness was elicited in the right upper quadrant of the abdomen, and the left costovertebral angle was markedly tender on Murphy's percussion. Homans' sign was not present. Blood studies showed a hemoglobin level of 10.9 Gm. per 100 cc. and a white blood cell count of 13,900 per cubic millimeter, with 76% neutrophils (56% mature and 20% band forms), 23% lymphocytes, and 1% eosinophils. The urine was cloudy, with a trace of albumin. The erythrocyte sedimentation rate was 0.5 mm. per minute and the carbon dioxide–combining power, 68 vol.%. The serum sodium level was 132 mEq. per 100 cc., the potassium level, 3.2 mEq.; and the chloride level, 105 mEq. The total serum protein level was 6.9 Gm. per 100 cc., with 3.8 Gm. of albumin and 3.1 Gm. of globulin. The guaiac test on stools was 1+. Repeated blood cultures were sterile. A throat culture grew numerous colonies of Diplococcus pneumoniae and Staphylococcus aureus. Culture of the sputum grew Pseudomonas aeruginosa (Bacillus pyocyaneus) in pure culture. No acid-fast bacilli or fungi were found. X-ray of the chest now disclosed pleural effusion on the left and an infiltration in the base of the right lung compatible with a pneumonic process. An electrocardiogram was interpreted as in keeping with left ventricular hypertrophy and sinus tachycardia (rate, 150 beats per minute). Result of a skin test for histoplasmosis was negative.

On the 21st hospital day, the patient's condition deteriorated and his temperature rose to 104 F (40 C). On examination of the chest there were harsh respiratory sounds and coarse crepitant rales in the base of both lungs. The heart rate was 160 beats per minute and regular. The liver was palpable 2 fingerbreadths below the right costal margin. Digitalis and massive doses of several antibiotics were administered without any response.

One thousand cubic centimeters of blood were transfused, after which the hemoglobin level was 9.7 Gm. per 100 cc. The platelet count was 200,000 per cubic millimeter, and the leukocyte count was 24,750, with 90% neutrophils (including 22 band forms). A bone marrow aspiration, smear, and culture were reported as normal. No tumor cells were found in the sputum.

On the 24th hospital day, the patient suddenly developed increasingly severe dyspnea and cyanosis. The blood pressure was unobtainable and the pulse became thready, at a rate of 160 beats per minute. Respirations were gasping, at 50 per minute. He then lapsed into coma, stiffened up in bed, and died at 10:25 a. m.



Section from urinary bladder showing organized thrombus partially attached to venous intima by proliferative endothelium (×250).

Autopsy Findings.—At autopsy, the parietal pleura on both sides was dull and congested and the lower lobe of the left lung was covered by fibrin. The heart weighed 310 Gm. The right atrium was slightly dilated, as was the right ventricle, where many antemortem clots ranging in size from 0.5 to 1.5 cm. were imbedded between the muscle columns. The underlying endocardium did not appear thickened. Sections of the ventricles revealed no grossly visible disease of the myocardium. The valves and coronary arteries appeared to be normal. The lungs were relatively heavy, the right lung weighing 720 Gm. and the left 710 Gm. Large granular brownish-red clots filled the branches of the pulmonary arteries of both lungs, and a cylindrical embolus, about 7 by 0.6 cm., lay free in the left pulmonary artery. The lower lobe of the right lung was enlarged, dark red, and covered by a thin film of fibrin. The middle and upper lobes of the right lung were still air-containing and light pink in color. Multiple sections of the lower lobe of the right lung revealed oozing dark-red surfaces. The left lung showed an area of infarction in the lower segment of the upper lobe. The lower lobe was completely solidified and dark red in color; it sank in water. Multiple sections of the lower lobe of the left lung appeared essentially similar to those of the lower lobe of the right lung. No abnormality was seen in the airways. In the midportion of the left kidney there was an area of recent infarction, 1 cm. long by 0.2 cm. wide, yellowish in color. Milking of the lower extremities while observing the exodus at the inferior vena cava failed to produce any movable clots.

Microscopic examination of the lungs revealed organized clots in the branches of the pulmonary arteries that were adherent to the intima of the vessels and exhibited fibrous tissue proliferation in continuity with the intimal layers. The presence of organized fibrin and fibroblast proliferation implied that some of the clots had been in situ for several days. Organized clots without mural attachment lay within the pulmonary arterioles in areas of widespread infarction. Several blocks showed infarcted lung tissue. The myocardium of the left ventricle was histologically normal. In the wall of the right ventricle there was a mural thrombus in situ without demonstrable attachment to the endocardium. The perivesical and intramural veins of the urinary bladder contained organized thrombi partially attached to the venous intima by proliferative endothelium (see figure). The prostatic venous plexus was extensively involved microscopically by thrombus formation. One large vein showed a recent thrombus of the same structure as those found in the lungs and right heart. Other veins exhibited organized fibrous obliteration with recanalization. The kidney exhibited foci of interstitial hemorrhage and areas of recent infarction.

Comment

Serious or fatal pulmonary emboli may arise from the venous system of apparently normal adolescents and may be the first manifestation of asymptomatic phlebothrombosis.

Although the underlying cause of phlebothrombosis still remains obscure, Crane[5] has postulated that sudden and repeated muscular efforts and strains may in some individuals cause thrombosis of the deep lower leg veins and, in turn, of the pelvic veins. Prolonged dependency stasis, imposed by airplane flights, automobile rides, and even attendance at the theater, has been known to induce thrombosis of this sort, as reported by Homans.[6]

In the present case, some of the emboli apparently originated from the prostatic venous plexus, a rather common site of origin. In 147 cases of pulmonary emboli Moran[7] encountered 44 (29.9%) arising from the prostatic venous plexus.

The symptoms and signs of pelvic venous thrombosis are rather vague and seldom adequately evaluated, as DeTakats and Fowler[8] have shown. They may, however, include pain and swelling of the buttocks or in the abductor muscles close to the inguinal fold, associated with sciatic neuritis, frequency of urination, and mucous diarrhea, or slight suprapubic edema and palpable cords lateral to the prostate or uterus, although none of these criteria were observed in this case.

The manifestations of pulmonary embolism are exceedingly varied and have a definite tendency to recur.[9] Dyspnea is one of the most prominent symptoms. In the present case dyspnea was of sudden onset and rapidly progressed to gasping respirations resembling intermittent episodes of hyperventilation accompanied by extreme restlessness. Mental confusion, marked apprehension, and fright were conspicuous to the extent that a psychiatric consultation was requested. Savacool and Charr[10] reported 12 cases of pulmonary thrombosis in which mental confusion, presumably attributable to cerebral ischemia, was most striking. Other predominant symptoms in the present case were fever, cyanosis, chest pain, tachycardia, anemia, and rapidly progressing signs of right heart failure.

Summary

In a fatal case of multiple pulmonary embolism in a 15-year-old boy, intensive and prolonged physical exertion appeared as the etiological factor. Frequent episodes of hyperventilation were observed.

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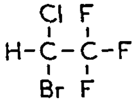
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Halothane (Fluothane).—2-Bromo-2-chloro-1,1,1-trifluoroethane.—The structural formula of halothane may be represented as follows:



$$\begin{array}{ccccc} & & Cl & & F \\ & & | & & | \\ H & - & C & - & C - F \\ & & | & & | \\ & & Br & & F \end{array}$$

Actions and Uses.—Halothane, a volatile, noninflammable liquid, is a general anesthetic agent. Its potency, based on maintenance concentrations of inhaled vapor, is variously estimated as four times that of ether and one-half to twice that of chloroform. The high potency of halothane, which is the basis of many of its desirable properties as an anesthetic agent, is at the same time a serious hazard, necessitating the greatest care and precision in its use. It should be administered only by thoroughly trained individuals who are familiar with its pharmacology and toxic potentialities and with the techniques indicated for its administration.

Induction with halothane is smooth and rapid. Vapors of anesthetic concentration are not unpleasant to most patients and do not irritate the mucous membranes. Halothane depresses, rather than stimulates, salivary and mucous secretions. Sensory depression in the first stage of induction is rather poor. A brief period of excitement is not infrequent, particularly if premedication is light, but is less troublesome than that produced by most other inhalation anesthetics. Complications during induction such as coughing, laryngospasm, bronchospasm, and vomiting are uncommon. When halothane is used for induction, surgical anesthesia is usually achieved in 2 to 10 minutes. The pharyngeal and laryngeal reflexes are obtunded very early, and the relaxation of the jaw is excellent. Therefore, endotracheal intubation may often be done without the use of relaxants, even under very light anesthesia. However, the rapid reversibility of halothane anesthesia requires that the intubation be accomplished swiftly.

Some degree of hypotension occurs in most patients during anesthesia with halothane and constitutes one of the major limiting factors in its use. The blood pressure is lowest during the induction period; during surgical anesthesia it may return to normal but usually stabilizes at a level still somewhat below preinduction values. The degree of hypotension seems to be proportional to the concentration of the vapor in the inspired mixture; sudden increases in this concentration often precipitate a profound fall in blood pressure. Similarly, increasingly severe hypotension may attend attempts to reach lower planes of anesthesia. The mechanism by which this hypotension is produced is unknown. The appearance of the skin, which is dry, warm, and pink, and with distended veins, suggests peripheral vasodilation. Considerable evidence has been adduced in support of a ganglionic blocking effect, but this is not universally acccepted. Evidence concerning other proposed mechanisms is also conflicting or inadequate.

Halothane not infrequently produces alterations of cardiac rate and rhythm. The most common of these is bradycardia; this, in some patients, may be quite marked; heart rates as low as 30 per minute have been reported. Fortunately, this complication can usually be prevented by the prior administration of adequate doses of atropine or other anticholinergic agents. Other disturbances that have been reported include atrioventricular nodal rhythm, atrioventricular dissociation, shifting pacemaker, extrasystoles of ventricular origin, bigeminal and trigeminal rhythms, and cardiac arrest. Deeper levels of anesthesia are associated with a higher incidence and greater severity of these reactions.

Like cyclopropane and chloroform, halothane unquestionably sensitizes the myocardium to the action of epinephrine and levarterenol. Injection of these amines during halothane anesthesia may induce ventricular tachycardia or fibrillation. On the other hand, no serious arrhythmias have accompanied the use of phenylephrine, methamphetamine, or methoxamine. There is some evidence from animal experiments that halothane decreases the force of ventricular contraction. Whether this occurs during halothane anesthesia in human patients is unknown. It seems unlikely, at least, that halothane produces the profound depression often seen with chloroform.

Halothane often causes a diminution in respiratory minute volume. This depression becomes progressively more severe as anesthesia is deepened. Respiratory movements are typically quite shallow, whereas the rate may be either increased or decreased. A pronounced tachypnea has been reported. At levels of anesthesia below the second plane, many patients require respiratory assistance. Completely controlled respiration is said to be achieved with unusual ease.

As with ether, and unlike the situation prevailing with use of chloroform, the circulation usually remains functional at the point at which complete respiratory paralysis occurs. The blood pressure is usually adequate, and the heart may continue to beat for several minutes after respirations cease. Consequently, in such cases, discontinuance of halothane anesthesia and administration of oxygen by artificial respiration is ordinarily followed by rapid lightening of the level of anesthesia and resumption of spontaneous respiratory activity.

Even at very shallow levels of anesthesia, halothane inhibits both the painless uterine contractions of late pregnancy and the contractions during labor, whether spontaneous or induced by oxytocics. The effect has been compared to that of deep ether anesthesia. Severe hemorrhage that has occurred during cesarean sections performed under halothane anesthesia may possibly be due to this effect on uterine tone.

Muscular relaxation in halothane anesthesia is only moderately good. Since the depth of anesthesia is limited by the effects of halothane on the heart and circulation, a skeletal muscle relaxant must often be used as an adjuvant in operations on the upper abdomen or when the peritoneal cavity is to be opened. Succinylcholine, decamethonium, and gallamine have been satisfactory for this purpose. Gallamine possesses the added theoretical advantage of inhibiting the action of the cardiac vagus and thus may help to minimize the bradycardia produced by halothane. Tubocurarine, on the other hand, has produced profound and irreversible hypotension in animals anesthetized with halothane; therefore, tubocurarine probably should not be employed in human patients until further studies clearly establish its safety.

A number of other drugs have been associated with unusual and undesirable effects when given during halothane anesthesia. Since these effects have been noted in only single or, at most, a few instances, and since surgical procedures themselves may modify response to drugs, it is uncertain that halothane is responsible for the modified response. Nevertheless, the following observations seem pertinent. Unusual sensitivity to the hypotensive effect of hexamethonium was reported; an adequate blood pressure was difficult to maintain in a patient who had been taking reserpine; chlorpromazine given postoperatively to control shivering was followed by a sharp fall in blood pressure. These three observations, together with the known propensity of halothane to cause hypotension, enjoin caution in the use of hypotensive agents in conjunction with this agent. Increased sensitivity of a diabetic to insulin after halothane anesthesia has also been reported.

The rapidity of recovery from halothane anesthesia is one of the most valuable attributes of the drug. Reflexes begin to reappear within two minutes and spontaneous movements within five minutes. The incidence of vomiting, which occurs in about 5% of patients in the immediate postoperative period, is unusually low. With proper dosage there is no prolonged period of postoperative hypotension. Intense shivering, apparently associated with a rather pronounced fall in body temperature, is a fairly common occurrence.

Because of its chemical structure, that of a halogenated hydrocarbon, early investigators feared that halothane would have deleterious effects on the liver, similar to those produced by chloroform. To date, however, no reports of serious or permanent hepatic damage have appeared. Liver function tests indicate that halothane, like other anesthetic agents, may produce a temporary depression of hepatic function, but that this effect is transitory, and return to normal usually occurs within a week. The incidence and severity of the hepatic depression is comparable to that produced by ether or cyclopropane. Although histological studies in animals have revealed minimal depletion of glycogen and mild fatty changes, necrosis or other severe morphologic changes have not been detected.

Neither histological studies nor renal function tests have revealed any serious untoward effect on the kidney.

The administration of halothane should be restricted to qualified anesthesiologists. It should be employed only in carefully selected cases and should not be regarded as a general-purpose substitute for ether, cyclopropane, or other standard anesthetic agents. The use of halothane in operations requiring a considerable degree of muscular relaxation is illogical, since its relaxant effect is poorer than that of ether and no better than that of a number of other less hazardous anesthetic agents. Halothane should not be used in the presence of shock, severely diminished cardiac reserve, serious cardiac arrhythmias, or when injection of epinephrine or levarterenol is contemplated. Its use in obstetrics for normal or cesarean deliveries is accompanied by the danger of uterine relaxation and increased bleeding.

The noninflammability of halothane may render it especially useful when electrocautery is used and when diagnostic radiological procedures are carried out. In thoracic surgery, the ease with which controlled respiration can be instituted and its depression of secretions and lack of irritation of the mucosa may be regarded as desirable properties. Lack of elevation of the cerebrospinal fluid pressure and cerebrovenous pressure during halothane anesthesia may indicate its choice for certain neurosurgical procedures.

Dosage.—Halothane is given by inhalation. The extreme potency of the agent and the rapidity with which it produces changes in the level of anesthesia make it essential to exercise extreme care in administration. Unusually swift and accurate appraisals of the clinical signs of the depth of anesthesia must be made as a basis for controlling the concentration of halothane being inspired by the patient. Signs of anesthesia with halothane resemble those with ether, but the successive stages are traversed much more rapidly. Moreover, the pupils constrict early in, and remain constricted throughout, the stage of surgical anesthesia.

Halothane has been administered successfully by a number of techniques: semiclosed, with circle or to-and-fro carbon dioxide absorption; direct flow, without carbon dioxide absorption; and direct flow, nonrebreathing. If sufficient care is taken, halothane can be given by the open-drop method for the induction of anesthesia in children; this, however, is not a preferred method of administration. Difficulty has been reported with the completely closed circuit with carbon dioxide absorption, presumably because of the impossibility of estimating the concentration of halothane being inhaled at a given moment.

The controls provided by conventional ether vaporizers are frequently too coarse to provide sufficiently fine gradations in the amount of vapor delivered. Special vaporizers are now available, with highly accurate settings or calibrations designed to deliver constant concentrations in the presence of variable conditions of temperature, agitation of the vaporizer, changing fluid levels, and varying rates of flow.

Halothane itself, alone or in conjunction with nitrous oxide, may be used for induction. Concentrations of 2 to 2.5% vaporized by a flow of oxygen or nitrous oxide–oxygen mixtures are usually sufficient. A relatively high proportion of nitrous oxide in the mixture is favored by some anesthesiologists for the purpose of improving the analgesia in very light anesthesia. If preferred, however, other conventional agents, such as thiopental or nitrous oxide–oxygen (without halothane) may be used.

Once surgical anesthesia has been achieved, concentrations of 0.5 to 1.5% halothane are sufficient for maintenance.

Premedication before halothane anesthesia need not differ significantly from that used with other inhalation anesthetics. It is especially important, however, that an anticholinergic drug, such as atropine, be included to prevent or minimize bradycardia, which is a frequent concomitant of halothane anesthesia. If atropine is replaced by scopolamine, it should be remembered that the latter has only one-half the activity of atropine on the cardiac vagus.

Preparations.—liquid (inhalant) 125 cc.

Year of introduction: 1956.

Ayerst Laboratories, Division of American Home Products Corporation, cooperated by furnishing scientific data to aid in the evaluation of halothane.

THE JOURNAL
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INBORN ERRORS OF METABOLISM

THE influence of genetic make-up on the occurrence of human disease has been familiar to physicians from earliest times. Knowledge regarding the manner in which such influences operate has been available only more recently. The concept of "inborn errors of metabolism" was introduced by Sir Archibald Garrod in 1908.[1] He dealt with four specific metabolic disorders—albinism, alkaptonuria, cystinuria, and pentosuria.

His uncanny prediction that products excreted in these diseases were in reality normal metabolites which accumulated because of deficiency of enzymes responsible for further metabolism has been amply confirmed in recent years. The few diseases studied by Garrod were long considered medical rarities of esoteric interest. With the unraveling of the mysteries of intermediary metabolism, these diseases assumed new importance and have indeed aided in the comprehension of metabolic pathways. The excretion of homogentisic acid in alkaptonuria and 1-xylulose in pentosuria were of immeasurable help in delineating the metabolism of the aromatic amino acids and contributing to the understanding of carbohydrate metabolism. As more modern enzymatic techniques have become available, direct demonstration of enzymatic deficiencies has become possible.

Since Garrod's original contributions many other diseases have been added to the ever-growing list of "inborn errors of metabolism." Taken together they no longer represent medical rarities.

The concept of inherited metabolic abnormalities has been broadened in recent years. The finding by Pauling and associates[2] that the hemoglobin of patients with sickle-cell disease differs from normal adult hemoglobin opened a whole new field of understanding of human disease. Subsequent studies[3] have established that hemoglobin of different persons differs chemically with respect to the presence of a particular amino acid at specific locations in the polypeptide chain. It is apparent that genetic variation may result in the synthesis of proteins closely related to normal but varying in critical detail. Changes in such detail may vastly alter biological function. The apparent absence of a given enzyme may be due, in fact, to the synthesis of an abnormal molecule which lacks enzyme activity.

Many of the metabolic abnormalities appear to be recessive characteristics, thus the full expression of the disease occurs only in homozygotes. Of great interest, however, has been the recent demonstration of many examples of partial expression of some metabolic defects in some heterozygotes. For example, it is known that heterozygotes have about 40% hemoglobin S (sickle-cell hemoglobin) in their erythrocytes. The finding of partial expression in heterozygotes opens up new possibilities that genetic variation may account for more subtle individual metabolic differences.

The metabolic anomalies studied by Garrod were of such a nature as to be detectable from the time of birth. It is, however, apparent that other heritable defects may become manifest only later in life. Typical of such a disease is diabetes mellitus. Evidence for the heritable nature of this disease has been available for many years. There is yet no explanation for the nature of the metabolic defect which permits this disorder to appear at variable ages. There is reason to believe that some metabolic abnormality occurs before the more familiar manifestations of the disease appear.

That a heritable defect resulting in a metabolic abnormality may only become evident after an elapse of time has profound medical implications. It is possible that other diseases have a similar underlying etiology.

It is now obvious that the concept of inborn errors of metabolism is of importance far beyond a few rare syndromes. Further research in enzymology and human genetics will undoubtedly result in rich rewards in the understanding of human disease.

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MEDICINE AND THE LAW

OPINION OF THE JUDICIAL COUNCIL

The Judicial Council has authorized the publication of the following opinion.

Question: The 1946 report of the Judicial Council states, in part, that "The division of income given to members of a group practicing jointly or in a partnership must be in proportion to the value of the services contributed by each individual participant." The 1947 report of the Council states, "Since the principles of ethics for private practice absolutely forbid the splitting of fees under any and all circumstances, the same rule applies to group practice; and the group formed must be a real partnership in which the total income is divided not equally but according to the individual income earned by the member." Do these reports mean that only the medical services rendered by a member of a group or partnership may be considered in arriving at the amount payable to each participant?

Answer: In order to clarify its position with respect to the division of group or partnership income the Judicial Council approves and publishes the following rephrasing of its 1946 and 1947 reports on this subject:

> The division of income among members of a group, practicing jointly or in partnership, may be determined by the members of the group and may be based on the value of the professional medical services performed by the member and his other services and contributions to the group.

GOVERNMENT SERVICES

AIR FORCE

School of Aviation Medicine Moved.—The Air Force School of Aviation Medicine moved in July from Randolph Air Force Base, northeast of San Antonio, Texas, to new quarters at Brooks Air Force Base, on the southern edge of the city. This is the second time in its 41-year history that the school has moved to Brooks. More than 33 years ago the school moved there from Mitchell Field, Long Island. Of the seven structures comprising the new facility, five are strictly for aerospace medicine research and instruction. The largest of these is the four-story centrally located Research Institute Building. Conveniently close are the Research Laboratory Shops, Altitude Laboratory, Academic Building, and Flight Medicine Laboratory. To the rear of the group are the heating and cooling plants. The move was incomplete, and priority projects now under way will keep a portion of the school's department of physiology-biophysics at Randolph until winter.

The most outstanding improvement Brooks has over the Randolph facilities is vastly increased classroom space in the academic building. At Randolph the school had six classrooms with a total seating capacity of 279. The Brooks school will have 16 modern, fully equipped classrooms with seats for 735 students, plus a 433-seat assembly hall. In addition it will be partially equipped with closed-circuit television. In connection with these expanded educational facilities, some of the courses previously offered at the Gunter Air Force Base, Ala., branch of the school will be transferred to Brooks. The flight nursing course, six weeks in length and with a total of about 330 students each year, is one of these. All told, the School of Aviation Medicine at Brooks will graduate about 950 students each year from its courses.

A special feature of the new school is the shop for making contact lenses—the only one of its kind in the Air Force. The department of biometrics will have an "electronic brain" for quick analysis of complex scientific statistics. The ear, nose, and throat department will have a reverberation chamber, a room that reflects and intensifies sound, which will be used to study the effects of noise on human beings and animals. The department will also have an anachoic chamber, a room which absorbs sound. It is so quiet in this room that a person can hear his own heartbeat. The room will be used for a variety of purposes, including the testing of delicate hearing instruments and the clinical evaluation of patients with hearing difficulties. The department of radiobiology will have a high-level cobalt-60 radiation facility shielded on all sides by about 5 ft. of concrete. Advanced x-ray equipment will be installed in the flight medicine laboratory. The research photography laboratory will have a full-scale motion picture studio with a sound stage, as well as closed circuit television capabilities.

The space medicine division is scheduled to receive a two-man space cabin simulator in October. It will be capable of sustaining two men for up to 30 days without outside help. The second floor of the Research Institute will have small cubicles where researchers and students can study and write in peace and quiet. The institution's 47,000 volume library will also be here. The third floor will house laboratories for pathology, toxicology, space medicine, pharmacology, and radiobiology. Among buildings planned for the future are a library and professional building.

NAVY

Personal.—Rear Adm. James R. Fulton, M. C., U. S. N., was retired in June after 34 years active service. His last assignment prior to retirement was district medical officer, Fourth Naval District.——The following captains of the medical corps were retired on July 1: Benjamin Ahl, O. H. Alexander, R. W. Babione, W. C. Baty Jr., C. E. Bentel, W. L. Berkley, T. D. Boaz, T. J. Carter, R. E. Fielding, J. R. George, J. N. C. Gordon, J. H. L. Heintzelman, L. L. Kenney, H. M. Maveety, L. E. McDonald, R. S. Simpson, P. E. Spangler, G. E. Stahr, W. P. Stephens, C. B. Stringfellow, J. R. Weisser, O. W. Wickstrom, M. R. Wirthlin, O. D. Yarbrough, and C. K. Youngkin.——The following retired captains of the medical corps who had been serving on active duty reverted to inactive status: J. M. Amberson and L. B. Marshall.

VETERANS ADMINISTRATION

Home-Town Medical Program.—New contracts for the fiscal year 1960 have been completed with medical association intermediaries for conduct of the Veterans Administration's home-town medical program in nine states. Because the contracts include provision for direct processing of physicians' billing statements by the VA, instead of through the intermediaries as in the past, the agreements are expected to expedite payment to private physicians involved and result in a saving of government funds. The nationwide home-town program allows veterans with service-connected disabilities to receive medical care at VA expense from nearly 38,000 private physicians of their choice in areas where care at VA outpatient clinics is not available. The states in which the new contracts have been signed with intermediaries—mostly Blue Cross-Blue Shield organizations—are California, Colorado, Hawaii, Michigan, New York, North Carolina, Oregon, Washington, and Wisconsin.

In the other 41 states and in the District of Columbia the program will continue to operate during the coming fiscal year under previous agreements with state medical associations and other arrangements, as it has in the past. On July 1, physicians from the nine states where the intermediary contracts have been signed began sending their bills for the program directly to VA offices, as is done by physicians in the program from other states.

Paper work for the VA home-town medical care program will be reduced substantially by a new system of mechanized record writing that became effective July 1. The new record writing system will also save time for private physicians in the program. Forms to be completed monthly by the doctors have been reduced to two—a report of treatment rendered and the doctor's bill to the VA for his services. Both are designed to make his writing job brief. The name and address of the private physician, the name and adress of the VA office handling the forms, and the name and VA claim number of the veteran receiving treatment will be printed on the forms by VA Addressograph plates. Use of window envelopes will make addressing of envelopes unnecessary.

The doctor also will receive from the VA an annual authorization for treatment for each of his patients in the program, valid for approved treatment during the year as needed. The VA advises doctors participating in the program to mail their treatment reports and billing statements together to the agency promptly at the end of each month. These forms will be machine-processed by a punch-card system at VA regional offices after medical approval.

PUBLIC HEALTH SERVICE

Dr. Anderson Retires.—Dr. Otis L. Anderson retired on July 1 after 30 years of active duty. Since Oct. 1, 1957, Dr. Anderson has been assistant surgeon general for personnel and training. Immediately on his retirement from the Public Health Service he joined the Washington office of the American Medical Association as medical liaison representative. His post in the Public Health Service was filled by Dr. Richard C. Arnold.

Personal.—Dr. Vernon Knight of Vanderbilt University Medical School, Nashville, Tenn., was appointed as head of the clinical research program of the National Institute of Allergy and Infectious Diseases where he will supervise the planning and conduct of patient-centered studies of diseases caused by viruses, bacteria, fungi, protozoa, and parasitic worms. A clinical program in allergy is also envisioned. The clinical research program will stress staphylococcic infections, especially those due to antibiotic-resistant strains.

MEDICAL NEWS

COLORADO

Dr. Hildyard Named Division Head.—Dr. Victor H. Hildyard, of Los Angeles, was appointed assistant professor and head of the division of otolaryngology, department of surgery, University of Colorado School of Medicine, Denver. Dr. Hildyard assumed the position July 1. He has been in the private practice of otology at Los Angeles since 1957, where he was clinical instructor in the specialty at the University of Southern California.

Plan Hospital for Progressive Patient Care.—Plans for the construction of a new 8-million-dollar, multiphased hospital unit for the Sisters of Mercy of Colorado were announced by Sister Mary Miguel, administrator of Mercy Hospital, Denver. The new eight-story 500-bed hospital will occupy the entire city block on the present site of Mercy Hospital at East 16th Avenue and Milwaukee Street. The progressive patient care plan calls for divisions of "intensive," "intermediate," and "convalescent" care as determined by the degree of illness of the patient admitted to the hospital. The seriously ill patient will be placed in an intensive care unit, with a specially trained nurse available. The convalescent care units will enable the patient to move about freely and assist in meeting his own needs. The present south wing of Mercy Hospital will be converted into a 200-bed hospital home for senior citizens, including small apartments for retired couples needing some medical supervision. Facilities will include rehabilitation, occupational therapy, recreational and central dining area for ambulatory guests. Among the innovations to be used in the new project is a system of electronics in the operating rooms and delivery rooms which will monitor each patient undergoing anesthesia. The present Mercy Hospital was begun in 1901.

CONNECTICUT

Fund to Honor Dr. Barker.—The Associates of the Yale Medical Library announce that the nucleus of a book fund was established at the Medical Library to honor Dr. Creighton Barker, New Haven, a member of the associates and a contributor to the library's collections. As a tribute to Dr. Barker, contributions to this fund are invited for which a suitable bookplate will be designed. Checks may be made payable to Yale University and mailed to Dr. Herbert Thoms, Yale Medical Library, 333 Cedar St., New Haven, Conn.

ILLINOIS

Deaths from Suicide.—*The Illinois Health Messenger* for June reported that deaths from suicide numbered almost one per 1,000 of the total deaths in Illinois in 1956, when suicide ranked 11th as a cause of death in the state. No reported deaths from suicide occurred among persons under age 15, but in the age group 15-24 there were 38 suicidal deaths. The age group with the largest total number of deaths from suicide was 45-64. In 1956, suicide in Illinois ranked sixth among the leading causes of death in persons 15-24, fourth in the 25-44 age group, and eighth in the 45-64 age group. Suicide was not among the leading causes of death among persons 65 years and over.

Chicago

University News.—Dr. George E. Miller, director of house staff education at Buffalo (N. Y.) General Hospital and associate professor of medicine at the University of Buffalo School of Medicine, was appointed to the newly created post of director of research in medical education at the University of Illinois College of Medicine. The new post calls for developing and administering a Commonwealth Fund grant of $112,000 received last November for a two-year pilot study of the process of educating a medical student. The study is expected to result in a permanent center for educational research at the college. Both Dr. Miller's appointment, with the rank of associate professor, and the grant become effective Sept. 1.——Dr. Orville T. Bailey, professor of neuropathology, Indiana University School of Medicine, Indianapolis, was appointed professor of neurology at the University of Illinois College of Medicine. Dr. Bailey succeeded Dr. Percival Bailey, Chicago, not related, who retires from the university Sept. 1. Dr. Orville Bailey is president-elect of the American Association of Neuropathologists and in this capacity was invited to lecture before the British Association of Clinical Pathologists in September.

Dedicate La Rabida Research Center.—Dedication ceremonies for the Richard J. Finnegan Memorial Building, housing the Variety Club Research Center, of the La Rabida Sanitarium were held June 13 and 14. The building, having laboratories

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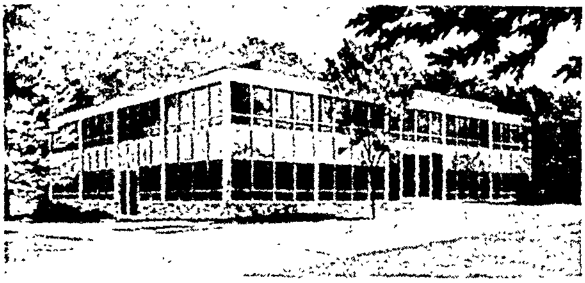
Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

equipped with modern chemistry, physics, and biology tools, has a library and conference room available for use by the medical and research staff of the hospital. The upper level of the building is devoted primarily to chemical laboratories including organic, physical, and biochemistry laboratories, and special rooms for instruments and isotope studies. The lower level is devoted to bacteriological experimentation, and includes animal quarters and animal research laboratories. Units are available for experimental pathology, microbiology, and immunology. The ceremonies included a scientific symposium June 13 and a public meeting on rheumatic fever June 14 at which Dr. Aims C. McGuinness, special assistant to the secretary, Health and Medical Affairs, U. S. Department of Health, Education and Welfare, presented the Harry Remer Memorial Lecture. The history of La Rabida began in 1893, when Spain chose a replica of the La Rabida Monastery at Palos for the Columbian Exposition, to commemorate the discovery of America. After the exposition, Spain presented the building to Chicago. In 1896, the Women's Board of La Rabida was formed and took over management of La Rabida. The board has continuously served to provide for sick children in Chicago since that time. At first La Rabida was concerned with the care of infants with diarrheal disease. In 1927, under Dr. Robert A. Black, La Rabida became a sanitarium for children with rheumatic fever. In 1944, when La Rabida became affiliated with the five medical schools of Chicago, clinical care was provided by the respective departments of pediatrics and medical student teaching was introduced. At that time the first board of trustees was organized, with Mr. Samuel Emory Thomason as chairman, who was succeeded on his death by Mr. Richard J. Finnegan. Mr. Finnegan died in 1955. Arrangements began in 1948 for the conversion of the sanitarium to a hospital. In 1949, an affiliation with the University of Chicago for research was inaugurated and in 1950 research laboratories were opened. On July 1, 1957, the La Rabida–University of Chicago Institute was created. The present program covers care for patients up to age 18 with rheumatic fever, rheumatic heart disease, rheumatoid arthritis, allied connective tissue diseases, nephritis, and nephrosis.



Richard J. Finnegan Memorial Building Variety Club Research Center of La Rabida Sanitarium.

Conference on Heart Research.—"Heart Research in Industry" is the title of the seventh annual Heart-in-Industry Conference, which will be held Oct. 16 at the Sherman Hotel, Chicago. The sessions will focus on the significant contribution that industry can make in collaboration with medical science. Among the featured speakers will be Dr. James Watt, director of the National Heart Institute; Dr. Irvine H. Page, director of research, Cleveland Clinic Foundation; and Mr. A. Pope Lancaster, vice-president, manufacturing, Western Electric Company. There will be six workshop discussion groups with panelists representing labor, management, medical research, industrial medicine, and nursing. The conference is jointly sponsored by the Chicago Heart Association and the Association of Commerce and Industry. The conference chairman is Dr. Andrew J. Oberlander, leader of the Industrial Medicine Committee of the Chicago Heart Association, which is responsible for planning the meeting. Reservations should be sent to the Association of Commerce and Industry, 30 W. Monroe St., Chicago 2.

MAINE

State Medical Election.—Officers of the Maine Medical Association for 1959-1960 are: president, Dr. Allan Woodcock, Bangor; president-elect, Dr. Wilson H. McWethy, Augusta; executive director, Dr. Daniel F. Hanley, Brunswick; and secretary-treasurer, Dr. Esther M. Kennard, Brunswick. Dr. Eugene E. O'Donnell, Portland, is immediate past-president. Dr. Carl E. Richards, Alfred, is Council chairman.

MARYLAND

Semiannual Meeting in Ocean City.—On Sept. 18, the Medical and Chirurgical Faculty of the State of Maryland will hold its semiannual meeting in Ocean City, with headquarters at the Commander Hotel. The Council will meet the morning of Sept. 17, and the House of Delegates, the morning of Sept. 18. The speaker at the scientific session will be Dr. Roy Hertz, chief, Endocrinology Branch, National Cancer Institute, Bethesda, who will present, "The Chemotherapy of Hormone Producing Tumors." A dance is planned for the evening of Sept. 18. For information write Mr. John Sargeant, 1211 Cathedral Street, Baltimore 1, Executive Secretary.

MASSACHUSETTS

Dr. Joslin Honored at Doctor-Clergy Dinner.—The first annual Beloved Physicians Award of the Massachusetts Council of Churches was presented to Dr. Elliott P. Joslin, Boston, as the finale to a symposium held April 8 under the sponsorship of the Boston Council of Churches and the Department of Pastoral Services of the Massachusetts Council of Churches. In presenting the award to Dr. Joslin it was stated that "despite the different professional paths taken by physician and minister, both stand together in reverence for life and in awe of death." Dr. Edward D. Churchill, John Homans Professor of Surgery at the Harvard Medical School, represented the medical profession at the symposium and Rev. Samuel Miller, pastor of the Old Cambridge Baptist Church and newly appointed dean of the Harvard Divinity School, represented the clergy at the symposium.

MICHIGAN

Dr. Kramer Resigns.—Dr. Charles G. Kramer, Saginaw, resigned as secretary of the Saginaw County Medical Siciety. Dr. Arthur B. Thompson, of 2144 Ottawa, Saginaw, was appointed as secretary to fill the unexpired term. Dr. Kramer is moving to a different country.

Personal.—On June 18, Dr. James V. Neel, Ann Arbor, received an honorary doctor of science degree from the College of Wooster, Wooster, Ohio. —Dr. Roger B. Nelson, associate director of the University of Michigan Hospital, Detroit, was chosen president-elect of the Michigan Hospital Association which represents about 225 hospitals throughout the state.

Triennial Reunion in Ann Arbor.—The University of Michigan Medical School, Ann Arbor, with over 5,000 living graduates will hold its seventh triennial alumni reunion Oct. 14-17. The program will be chiefly scientific in nature, with clinics, professional exhibits, reports on current medical research, and televised patient demonstrations over a closed-circuit color system. The major nonmedical activity will be the Michigan-Northwestern football game Oct. 17. In addition, there will be class reunions and tours of the university's 8½-million-dollar medical sciences building. The reunion will also help mark the 90th anniversary of the University Hospital, the nation's first to be owned and operated by a university in connection with its own medical school. The last U-M Triennial was held in September, 1956. Dr. John M. Sheldon, Ann Arbor, is chairman of program committee.

MISSOURI

Annual Psychiatric Meeting.—The 12th annual meeting of the Mid-Continent Psychiatric Association will be held Sept. 18-20 at the Holiday Inn Hotel, St. Louis County. Dr. Addison M. Duval, director of the Division of Mental Diseases for Missouri, will address the opening session. Twelve scientific papers will be presented, including the following by out-of-town speakers:

Cerebral Vascular Insufficiency, Dr. Adolph L. Sahs, Iowa City.
Psychological Reactions to Trauma, Dr. Herbert C. Modlin, Topeka, Kan.
Criminal Responsibility, Dr. Manfred S. Guttmacher, Baltimore.
Problems in Classification and Treatment of Depression, Dr. Charles Shagass, Montreal, Quebec.
Therapeutic Problems and Observations of Manic-Depressive Patients, Dr. Joseph B. Parker Jr., Durham, N. C.
Group Psychotherapy in Private Practice, Dr. John J. O'Hearne Jr., Kansas City, Mo.

An early-bird cocktail party will be given Friday evening, Sept. 18. On Saturday afternoon golf, tours, and other events will be available. The annual banquet will be Saturday evening. A program for ladies has been arranged. Nonmembers are cordially invited. For information write Dr. James N. Haddock, 950 Francis Place, Clayton 5, Mo.

NEVADA

Annual Meeting in Reno.—The 56th annual meeting of the Nevada State Medical Association will be held Aug. 19-22, together with the ninth conference of the Reno Surgical Society at the Mapes Hotel, Reno. The Aug. 20 session will be opened with an address by Governor Grant Sawyer, of Nevada. The program includes the following guest speakers: Drs. Donald E. Cassels, Chicago; William Dock, New York; Frank H. Mayfield, Cincinnati, president, Ohio State Medical Association; Michael E. DeBakey, Houston, Texas; Charles P. Larson, College of American Pathologists; Joe Vincent Meigs, Boston; and Hubertus Strughold, Randolph Field, Texas. Panel discussions are planned for the mornings of Aug. 21 and 22, with Dr. John W. Cline, San Francisco, serving as moderator. A banquet is planned for the evening of Aug. 21, with Paul A. Siple, D.Sc., scientific leader, Amundsen-Scott I. G. Y., South Pole Station, Washington, D. C., as the speaker. For information write Mr. Nelson B. Neff, P. O. Box 188, Reno, Nev., executive secretary.

NEW JERSEY

Organize Psychoanalytic Group.—The formation of the New Jersey Psychoanalytic Society, an affiliate of the American Psychoanalytic Association and the International Psychoanalytical Association, was announced at a meeting of the society, June 13. The society, formed April 26, became the 20th affiliate society of the American Psychoanalytic Association. The officers elected at the first meeting of the society May 3 are: president, Dr. Herman Shlionsky, Montclair; vice-president Dr. Raymond H. Gehl, Newark; secretary, Dr. John E. Hughes, Trenton; treasurer, Dr. Samuel A. Weiss, Orange; representative of the executive council of the American Psychoanalytic Association, Dr. Benedict J. Bernstein, Elizabeth; and alternate representative, Dr. Howard H. Schlossman, Englewood. The present mailing address of the society is 377 S. Harrison St., East Orange, N. J.

NEW YORK

Fellowships for Research.—The University of Rochester established a program of postdoctoral fellowships to be awarded graduates of approved medical schools to enable them to pursue research in any of the departments of the School of Medicine and Dentistry. The Buswell Fellowships, made possible by the bequest of the late Mr. Ralph Hochstetter, are intended to assist "well qualified" doctors of medicine to prepare for academic careers. Buswell Junior Fellowships will be awarded to medical graduates who have completed one year of internship or equivalent training. Research experience is not required. Junior fellows are expected to spend about 90% of their time in research or advanced study in preparation for research. Junior fellowships will provide a basic stipend of $4,500 to $6,000 per year, depending on training and experience, and may be renewed with increments for a second or third year. An additional sum of $500 per year may be provided for each dependent. Buswell Senior Fellowships will be awarded to medical graduates who have held a Buswell Junior Fellowship for two or three years or have had comparable experience in medical research and wish to continue in an academic career. Senior fellowships will provide a basic stipend of $5,500 to $8,000 per year, depending upon training and experience, with provision for annual increments. An additional sum of $500 per year may be provided for each dependent. Applications will be received any time. Awards will be announced periodically. A fellowship may be activated at any time during the year after announcement of award. Information and application forms may be obtained from the Chairman, Committee on Buswell Fellowships, Department of Medicine, University of Rochester Medical Center, 260 Crittenden Blvd., Rochester 20, N. Y.

New York City

Paraplegia Researchers Honored.—The Paralyzed Veterans of America, Inc., presented awards to two Columbia-Presbyterian Medical Center physicians, Dr. James B. Campbell and Dr. C. Andrew L. Bassett, for their work in paraplegia, at the 13th annual convention dinner of the PVA, July 22. The two physicians share the 1959 awards with Mr. Harry A. Schweikert Jr., PVA president, who was honored for his "outstanding leadership." Dr. Campbell and Dr. Bassett have been studying the regenerative potential of the severed spinal cord in animals. This research was financed by the Department of the Army, Office of the Surgeon General; National Institutes of Health; the Playtex Park Research Institute; and the United Cerebral Palsy Research and Educational Foundation, Inc. Dr. Campbell is assistant professor of neurosurgery, and Dr. Bassett is assistant professor of orthopedic surgery.

Personal.—Dr. Murray Davidson was appointed director of the department of pediatrics of the Bronx Hospital. He will start his new full-time post Sept. 1. Dr. Davidson also was named associate clinical professor of pediatrics at Albert Einstein College of Medicine.——Dr. George James was named first deputy commissioner of the New York City Department of Health, replacing Dr. Roscoe P. Kandle, who left the department to become commissioner of health of New Jersey. Dr. James has served as a deputy of the health department in charge of planning and research since October, 1956.——The president of Peru, Mr. Manuel Prado, recently conferred the decoration of "Order of the Sun" rank of commander on Dr. George T. Pack, New York surgeon. The ceremony was held in Lima, Peru, on the occasion of the first Peruvian Cancer Congress. The Order of the Sun was founded by General San Martin in 1821.

NORTH CAROLINA

University News.—Dr. Joseph C. Aub, of Boston, delivered the Nathalie Gray Bernard lectures at Bowman Gray School of Medicine, April 30 and May 1, entitled "Cancer and Normal Cell Growth," and "Our Present Study of Cancer Growth." Dr. Aub also spoke at the annual banquet of the Bowman Gray Chapter of Alpha Omega Alpha, April 29. The Nathalie Gray Bernard Lectureship was established by the Bowman Gray faculty in 1942 in honor of Mrs. Bernard, one of the school's chief benefactors.

Annual Conferences on Aging.—The first of four annual conferences on gerontology will be held at Duke University, Durham, Nov. 19-21, under the sponsorship of the university's Center for the Study of Aging. The conference will emphasize basic biological and medical aspects of aging. The program will be built around lectures by some 10 guest speakers from medicine and science. Dr. Ewald W. Busse, director of the Duke Aging Center, noted that the conference is being planned primarily for physicians and persons with special interests in gerontology. The over-all series of four conferences will give equal attention to the biological-medical aspects of aging and to the social and behavioral aspects, with two alternate year meetings on each theme. Major papers and formal discussions of the conferences will be published.

Personal.—Dr. Eben Alexander Jr., professor of neurosurgery, Bowman Gray School of Medicine, Winston-Salem, and chief of professional services, N. C. Baptist Hospital, was reelected president of the United Medical Research Foundation of North Carolina. The foundation, which derives its income from United Funds and Community Chests in North Carolina, has contributed $171,215 to medical research in the state since it was founded four years ago.—Dr. Annie V. Scott, clinical professor of pediatrics, University of North Carolina School of Medicine, was presented with the annual Achievement Award by the Woman's Medical College of Pennsylvania, Philadelphia. The citation received by Dr. Scott reads, in part, "In proud recognition of her distinguished attainments as pediatrician and medical educator in China, where she served as a medical missionary for a large part of her life. . . ."

PENNSYLVANIA

Philadelphia

Dr. Ferguson Named Surgery Chairman.—Dr. Lewis K. Ferguson, professor of surgery, University of Pennsylvania Graduate School of Medicine, was appointed chairman of the department of surgery, effective July 1, succeeding Dr. Herbert R. Hawthorne, who has held the post since 1954. Dr. Hawthorne became an emeritus professor.

Hospital Completes Medical-Science Building.—The Lankenau Hospital had a schedule of events June 4-6 to celebrate completion of its new $4,300,000 Medical-Science Building. Brigadier General Carl W. Tempel, Washington, D. C., addressed a dinner in the hospital June 4. Lankenau's Medical-Science Building, a six-story structure, has three floors which contain 126 private and semiprivate bedrooms for short-term convalescent patients and others undergoing diagnosis or treatment for non-acute conditions. The new building also houses the recently expanded Division of Research, the Health Examination and Diagnostic Service, and an enlarged Physical Therapy Department. An "open house" was held June 6 for the general public.

Diplomat Takes Postgraduate Work.—Dr. Arturo Z. Pellerano, of Ciudad Trujillo, a physician representing the Dominican Republic in Philadelphia as its consul, was accepted for the University of Pennsylvania Graduate School of Medicine for the 1959-1960 school year. He will take courses toward obtaining specialty training in obstetrics and gynecology. Dr. Pellerano was appointed consul in Norfolk, Va., in June, 1957, after serving as medical director of the city hospital in Yabucoa, Puerto Rico. He received his M.D. degree from the University of Santo Domingo (Dominican Republic) School of Medicine in 1948, and completed his internship and residency at Yabucoa Hospital before becoming medical director.

University News.—At the annual meeting of the Hahnemann Medical College and Hospital's board of trustees May 27 Dr. Charles S. Cameron, dean, and Mr. Charles S. Paxson Jr., the hospital's administrator, were elected vice-presidents of the 111-year old Philadelphia institution.—Honorary degrees were presented at Hahnemann Medical College June 12 to Dr. Jonas E. Salk, Commonwealth Professor of Preventive Medicine, University of Pittsburgh; Dr. Stanhope Bayne-Jones, chairman, Secretary's Consultants on Medical Research and Education, U. S. Department of Health, Education and Welfare; and to Detlev W. Bronk, Ph.D., president, Rockefeller Institute for Medical Research. Dr. Bronk delivered the main address during the graduation program.

RHODE ISLAND

Symposium on Athletic Injuries.—The University of Rhode Island will present a symposium on the prevention and treatment of athletic injuries on Aug. 17-18 in Kingston. The symposium will include lectures, panel discussions, and demonstrations, with opportunities for questions and answers and participant discussion. Panel topics are Abdominal, Genitourinary, and Thoracic Injuries, and Conditioning the Player. The university will issue a certificate to all registrants who complete the symposium. Fee for the program is $25. For information and registration, write the University of Rhode Island, Department of Physical Education & Athletics, Kingston, R. I.

TEXAS

Symposium on Problems in Surgery and Medicine.—On Sept. 19, a symposium, "Current Problems in Surgery and Medicine," will be co-sponsored by the Fifth District Chapter of Texas of the American College of Surgeons, the Tenth District Medical Society of Texas, and the Beaumont Academy of Medicine. The meeting will be held at the Hotel Beaumont, in Beaumont. The following papers and speakers are scheduled:

Medical Evaluation of the Preoperative Surgical Patient, Dr. Michael J. Lepore, New York City.
Hysterectomy—*When and Why*, Dr. M. Edward Davis, Chicago.
Management of Severe Trauma of the Chest, Dr. Thomas H. Burford, St. Louis.
Five Year Follow-up of Extended Radical Mastectomy, Dr. Jerome A. Urban, New York City.
Peripheral Endarterectomy, Dr. Jack A. Cannon, Los Angeles.
Office Proctology, Dr. Robert Turell, New York City.

A program of ladies activities is planned. There is no fee for the meeting. For information write Dr. Bedford F. Pace, 555 Tenth St., Beaumont, Texas.

UTAH

New Headquarters for State Association.—Executive offices of the Utah State Medical Association and Salt Lake County Medical Society are occupying a newly remodeled and enlarged headquarters building at 42 S. 5th East. Work started last spring included an extension of the two-story structure, with a new facing of Park City sandstone and a complete revamping of the interior to provide more

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attractive and commodious quarters. A new feature on the first floor is an enlarged meeting room, with a movable partition and facilities for projecting slides or motion pictures. The second floor includes a new board room office for Mr. Harold Bowman, executive secretary, and other employees. Interior walls have been refinished with walnut paneling, and the structure has been refurnished and carpeted. A new heating and air-conditioning system was installed. Additional parking space in the rear has been installed.

VERMONT

Symposium on Catecholamines.—A symposium, "The Catecholamines in Cardiovascular Pathology," will be held at the University of Vermont College of Medicine, Burlington, Aug. 23-26. This symposium will be subdivided into three sections: (1) pathogenic mechanisms, (2) prophylactic possibilities, (3) rationale of therapeutic procedures. Both fundamental phenomena at the cellular level and clinical implications will be discussed to correlate basic and clinical points of view. Inquiries should be directed to Dr. Wilhelm Raab, Professor of Experimental Medicine, University of Vermont College of Medicine, Burlington, Vt.

VIRGINIA

Appoint Department Chairmen.—Administrative appointments at the Medical College of Virginia, Richmond, were announced by Dr. William F. Maloney, dean. These include professor and chairman of the department of medicine, Dr. William T. Thompson Jr., formerly chief of medicine at McGuire Veterans Administration Hospital, Richmond; professor and chairman of the department of pathology, Dr. George Margolis, formerly professor of pathology at Duke University School of Medicine, Durham, N. C.; professor and chairman of the department of psychiatry, Dr. Robert A. Senescu, formerly assistant clinical professor of psychiatry at Columbia University College of Physicians and Surgeons, New York City.

WEST VIRGINIA

State Convention in White Sulphur Springs.—The 92nd annual meeting of the West Virginia State Medical Association will be held at the Greenbrier, White Sulphur Springs, Aug. 20-22. The presidential address will be given by Dr. George F. Evans, Clarksburg. Governor Cecil H. Underwood will address the first general session the morning of Aug. 20, and Dr. Louis M. Orr, president, American Medical Association will be the guest speaker before the second session of the House of Delegates Aug. 22. Papers to be presented at the general sessions are as follows:

The Physician's Responsibility in the Prevention of Automobile Crash Injuries and Deaths, Dr. Fletcher D. Woodward, Charlottesville.
Abdominal Trauma with Emphasis on Automobile Injuries, Dr. Frederick E. Kredel, Charleston, S. C.
Injury in Sports, Dr. Owen B. Murphy, Lexington, Ky.
The Hyperventilation Syndrome, Dr. William A. Sodeman, dean, Jefferson Medical College, Philadelphia.
Must Time Take Its Toll, Dr. Theodore G. Klumpp, New York City.
The Clinical Diagnosis of Common Viral Diseases, Dr. Fred R. McCrumb Jr., Baltimore.
Habitual Abortion, Dr. Carl T. Javert, New York City.
Accidental Poisoning in Children, Dr. Julian P. Price, Florence, S. C., Vice-Chairman, A. M. A. Board of Trustees.
Radiation Hazards in Diagnostic Roentgenology, Dr. Harold S. Pettit, Charleston, S. C.

Tournaments for golf and trap and skeet shooting are planned. Motion picture sessions and technical and scientific exhibits are arranged. A program of entertainment is scheduled. For information write Mr. Charles Lively, 401 Atlas Building, Charleston, W. Va., executive secretary.

GENERAL

New Journal on Research of Sex.—The Society for the Scientific Study of Sex will publish a new journal, *The Journal of Sexual Research*. The first issue will appear early in 1960. The journal is to include original articles, reviews of the literature, book reviews, and abstracts covering the range of all the learned disciplines pertinent to the study of sex. Papers should be submitted to Hugo G. Beigel, Ph.D., 138 E. 94th St., New York 28.

Psychoanalytic Meeting in New York City.—The semiannual fall meeting of the American Psychoanalytic Association will be held at the Hotel Biltmore, New York City, Dec. 4-6. The program will feature about 25 scientific papers and four major panel symposiums on psychoanalytic aspects of medical practice. For information and reservations, write to the Executive Secretary, 36 W. 44th St., New York 36.

Call for Psychosomatic Papers.—The American Psychosomatic Society will hold its 17th annual meeting at the Sheraton-Mt. Royal Hotel in Montreal, Canada, on Saturday and Sunday, March 26-27, 1960. The program committee would like to receive titles and abstracts of papers for consideration for the program no later than Dec. 1. The time allotted for presentation of each paper will be 10 or 20 minutes. Abstracts, of two or three pages, in nine copies, should be submitted for the program committee's consideration, to the Chairman, Dr. Eric D. Wittkower, at 265 Nassau Road, Roosevelt, N. Y.

Meeting of Anesthesiologists.—The New England Society of Anesthesiologists will hold its second annual conference Sept. 17-19 at the Equinox House, Manchester-in-the-Mountains, Vt., under the theme, "Agents and Techniques." The following speakers will each present two papers: Dr. Paul R. Dumke, Detroit; Dr. Louis R. Orkin, New York City; Dr. Richard G. B. Gilbert, Montreal, Canada; Dr. William S. Howland, New York City; and Dr. Harold R. Griffith, Montreal, Canada. The annual golf tournament will be held the afternoon of Sept. 18, and the annual banquet, the evening of Sept. 19. For information write the New England Society of Anesthesiologists, P. O. Box 81, Kenmore Station, Boston 15.

Radiological Meeting in Denver.—The 21st midsummer radiological conference of the Rocky Mountain Radiological Society will be held Aug. 20-22 at the Hotel Shirley-Savoy, Denver. Dr. George A. Unfug, Pueblo, Colo., president of the society, will present an address at the opening session. The program includes the following guest speakers: Dr. Eugene P. Pendergrass, Philadelphia; Dr. Philip J. Hodes, Philadelphia; Dr. Owings W. Kincaid, Rochester, Minn.; Dr. Franz J. Buschke, San Francisco; and Dr. Magnus I. Smedal, Boston. At the banquet Aug. 21, 7:00 p.m., Dr. Hodes will present "Medical Meddlers; What Price Insecurity." Scientific and technical exhibits are scheduled, and a program of ladies' entertainment is arranged. There is no registration fee. For information write Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society News.—The officers of the American Gastroenterological Association are: president, Dr. H. Marvin Pollard, Ann Arbor, Mich.; president-elect, Dr. Hugh R. Butt, Rochester, Minn.; vice-president, Dr. Franz J. Ingelfinger, Boston; treasurer, Dr. George G. McHardy, New Orleans; and secretary, Dr. Wade Volwiler, Department of Medicine, University of Washington, Seattle 5, Wash. The annual meeting is scheduled for March 31-April 2, 1960, at the Roosevelt Hotel, New Orleans.——The following officers of the **Mid-Central States Orthopaedic Society** were elected in April to serve for the ensuing year: president, Dr. Harvey O. Anderson, Wichita; vice-president, Dr. Daniel L. Yancey, Springfield, Mo.; secretary-treasurer, Dr. Henry O. Marsh, Wichita; and members at large, Drs. Oscar P. Hampton Jr., St. Louis, and Dr. James E. Pollard, Pueblo, Colo.——Officers of the **Western Association of Physicians** are: president, Dr. David A. Rytand, San Francisco; vice-president, Dr. Paul Starr, Los Angeles, and secretary-treasurer, Dr. Wade Volwiler, Seattle.

Congress on Physical Medicine.—The 37th annual meeting of the American Congress of Physical Medicine and Rehabilitation will be held Aug. 30-Sept. 4, in Minneapolis. The American Academy of Physical Medicine and Rehabilitation will meet at the same time in a two-day seminar sponsored by the American Rehabilitation Foundation, a division of the Sister Elizabeth Kenny Foundation. Slated for discussion at the latter meeting are three basic subjects, including the hand and upper extremity, rehabilitation in speech and language, and basic research in the collagenoses. Five main sessions and scientific and technical exhibits will feature the five-day conference by the American Congress of Physical Medicine and Rehabilitation during the same period. Scientific films will deal with the management of muscular dystrophy, vocational status following chemopallidectomy for Parkinson's disease, and rehabilitation of the bilateral upper extremity amputee. Dr. Arthur C. Jones, Portland, Ore., is president of the American congress. He will address the assembly Sept. 2. The John Stanley Coulter lecture will be delivered by Dr. Robert L. Bennett, Warm Springs, Ga. Dr. Louis B. Newman, Chicago, is president of the American Academy of Physical Medicine and will be succeeded by president-elect Clarence W. Dail, Los Angeles. The congress is planning its third international session on physical medicine, to be held in Washington, D. C., the week of Aug. 21, 1960.

Infant Mortality.—The long-term downward trend in infant mortality has come to a halt, it is reported by statisticians of the Metropolitan Life Insurance Company. There were about 113,000 deaths among babies under one year of age in 1958, equivalent to a rate of 26.9 per 1,000 live births. This compares with the rate of 26.4 per 1,000 in 1957 and the all-time low of 26.1 in 1956 reported by the National Office of Vital Statistics. The record of the last two years is in contrast with that of the decade between 1945-1946 and 1955-1956, the statisticians point out. During that period every state, without exception, succeeded in reducing its infant mortality rate. In 31 states and the District of Columbia, the decrease amounted to 25% or more. New Mexico's infant mortality rate fell 56%, and Maine and West Virginia each recorded a reduction of over 40%. All of the major causes of infant mortality, except postnatal asphyxia, showed a decline during the decade ending in 1955-1956. The death rate from the gastrointestinal diseases dropped more than 60%. For whooping cough, the decline was about 75%. Other communicable diseases of childhood—measles, scarlet fever, and diphtheria—have been reduced "to vanishing proportions as causes of death in infancy." The improvement in mortality has been greater in later infancy, the statisticians report. For infants beyond one month of age, the death rate fell 40% between 1945-1946 and 1955-1956. For babies under 4 weeks of age, the decline was little more than 20%. For infants under one day of age, the death rate fell only 12%. Currently nearly two-fifths of all infant deaths occur in the first day of life; 10 years earlier the proportion was one-third.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	July 11, 1959		July 12, 1958
	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	2
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	2
Middle Atlantic States			
New York	3	6	..
New Jersey	2	2	4
Pennsylvania	1	1	..
East North Central States			
Ohio	4	10	..
Indiana	..	..	..
Illinois	2	2	2
Michigan	..	2	2
Wisconsin	..	..	..
West North Central States			
Minnesota	2	4	..
Iowa	13	22	..
Missouri	4	9	..
North Dakota	..	..	..
South Dakota	..	..	1
Nebraska	2	5	..
Kansas	3	11	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	4	5	1
West Virginia	..	..	7
North Carolina	4	4	2
South Carolina	1	2	1
Georgia	1	2	..
Florida	..	1	31
East South Central States			
Kentucky	1	1	..
Tennessee	3	3	3
Alabama	11	13	..
Mississippi	2	4	8
West South Central States			
Arkansas	14	16	..
Louisiana	2	4	2
Oklahoma	7	8	2
Texas	17	31	16
Mountain States			
Montana	..	..	12
Idaho	..	..	1
Wyoming	..	..	..
Colorado	1	1	..
New Mexico	..	1	2
Arizona	2	3	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	.	1	..
Oregon	..	..	1
California	5	5	9
Alaska	..	..	..
Hawaii	..	..	4
Puerto Rico	..	..	..
Total	111	179	108

Greeting Cards Aid Children.—Special modern greeting cards, UNICEF Greeting Cards, are published by the United Nations Children's Fund to "bring happiness, in the form of improved health and a better chance for survival, to countless needy children in underdeveloped areas of the world." In 1946 a 7-year-old girl was so grateful for the emergency aid she and her fellow school children had received from UNICEF that she tried to express their feelings by sketching a picture on a piece of glass. It was her effort which was to become the first UNICEF card. In 1949, 130,000 cards were purchased by friends of the Children's Fund in the United States. Last year, over 10,500,000 cards were sold in more than 70 countries and territories, half of them in the U. S. A. The profits from a single box of 10 cards priced at $1.25 can provide 45 children with a glass of milk every day for a week. Originally formed to supply emergency foods, mostly milk, to the children of war-torn Europe and Palestine, UNICEF is entirely devoted to the welfare of children and mothers. UNICEF is currently aiding more than 100 countries and territories in medical and nutrition programs, designed to become a permanent part of each country's health service. Each aided country matches the value of UNICEF supplies on an average ratio of more than $2 for each dollar of UNICEF aid. So far, with UNICEF's help, more than 103 million children reportedly have been vaccinated against tuberculosis; over 21 million persons, more than half of them mothers and children, have been cured of yaws; up to 1959, 3.9 million children reportedly had been saved from blindness. Each year, artists have donated their works to be reproduced as UNICEF Greeting Cards. This year they include Joan Miro, Dong Kingman, Jozef Domjan, Bettina, Doris Lee, and Kay Christensen. A descriptive brochure can be had by writing to the U. S. Committee for UNICEF, Greeting Cards, United Nations, N. Y.

Poliomyelitis Conference.—Sponsored jointly by the Pan American Health Organization and the World Health Organization, with the financial assistance of the Sister Kenny Foundation of Minneapolis, the International Conference on Live Poliovirus Vaccines in Washington, D. C., ended its sessions in June. Although the conference strongly urged continued use of the inactivated (Salk) vaccine, the members believe that there is a place for a vaccine that may be of lower cost, simpler to use, and potentially capable of having a greater protective effect on a community basis, specifically a vaccine that can be administered orally. It was recognized, however, that the use of a product that spreads beyond those originally vaccinated represents a radical departure from present practices.

More than 20 field studies were reported from 15 countries. Most of these were carried out in a highly susceptible population that had not been given the Salk vaccine. These studies yielded different results in different environments. For instance, in some studies the number of children who lacked antibodies and to whom the live vaccine had been administered, it was reported as being only 50 to 60% effective, whereas in others it was 90 to 100% effective. The degree of spread of infection to contacts of those vaccinated varied in different situations, but in families and in closed institutions spread was common. It has not been possible to follow clearly the natural spread of attentuated poliovirus after its first or second passage.

Studies of great magnitude involving administration of vaccine on a community-wide basis to hundreds of thousands of persons have been reported from Africa, Asia, Europe, Latin America, and the

USSR. Smaller, and therefore, more carefully controllable studies, have been reported from Europe and the United States. No evidence has been adduced that use of any of the vaccines has been followed by either paralysis or ill-defined illnesses in either group greater in number than have been observed in a control group or in the community at large among nonvaccinated persons. In most of the studies there have been no attempts to assess effectiveness other than by increase in antibodies. In a few instances, however, it has been claimed that use of the vaccine has been followed by low attack rates, either in those vaccinated or in the community, which are consistent with those that might be expected as a sequel to use of an effective vaccine.

CANADA

Duke of Edinburgh Installed.—Gowned in the robes of Chancellor of Edinburgh University, H.R.H. The Prince Philip, Duke of Edinburgh, following his installation as president of the Canadian Medical Association, is shown with representatives from other medical associations. Left to right: Sir Arthur Thomson, Birmingham, England, President, British Medical Association; H.R.H.; Dr. Louis M. Orr, Orlando, Fla., President, American Medical Association; Dr. R. Lemieux, Quebec City, P. Q., President-Elect, World Medical Association; and Dr. Emile Blain, Directeur-Général, L'Association des Médecins de Langue Francaise du Canada, Montreal, P. Q. The installation ceremonies took place at the Royal York Hotel, Toronto, and marked the 92nd annual general meeting of the Canadian Medical Association on June 30.

LATIN AMERICA

Society of Medical Education in Argentina.—The Argentine Society of Medical Education has been formed for the study of problems in medical education, with special and immediate emphasis on (1) the establishment of postgraduate residency systems in federal, municipal, and private hospitals; (2) modernization of the hospital system; (3) creation of specialty accreditation and recognition in the various medical fields, i. e., Argentine boards of internal medicine, boards of surgery, etc.; (4) collaboration with medical, scientific, and educational organizations with similar objectives. All correspondence should be directed to Dr. Jorge Manrique, Secretary, Cuemes 2926, Buenos Aires, Argentina.

FOREIGN

Pediatric Meeting in Budapest.—The Hungarian Pediatric Association will hold its biannual meeting on Nov. 26-29 in Budapest. Subjects will include: (1) Staphylococcus Infections, (2) X-Ray Injuries in Childhood, and (3) Hematological Diseases in Childhood. For particulars apply to Dr. Emil Litvay, Secretary General Péterfy Sándor utca 12, Budapest.

Congress of Gastroenterology.—The sixth meeting of the Association of the National European and Mediterranean Societies of Gastroenterology, organized by the Association of Dutch Gastroenterologists, will be be held in Leiden, the Netherlands, April 20-24, 1960. The main themes of the conference will be (1) pathology of the small intestine and (2) hepatitis, cirrhosis hepatitis, and their possible connection. Panel discussions, lectures and film shows will be arranged in connection with these themes and related subjects. Scientific and technical-commercial exhibits also will be organized. Original reports, either clinical or in the field of the basic sciences, are invited for submission and will be accepted for panel discussion or publication if approved by the scientific program committee. Titles for papers, together with a summary of not more than 200 words, should be sent not later than Aug. 1 to Dr. B. K. Boom, Congress Office, Department of Gastroenterology, University Hospital, Leiden, the Netherlands. The official language is English. Working languages will be English, French, German, and Spanish (with simultaneous translation). Registration fees (including an official reception, a banquet, and an excursion) are: Full members, U. S. $45; accompanying family members U. S. $20. After Nov. 1, the registration fee for full members will be U. S. $55. For information and registration forms, apply to the Congress Office, Sixth Meeting of the Association of the National European and Mediterranean Societies of Gastroenterology, Department of Gastroenterology, University Hospital, Leiden, the Netherlands.

CORRECTION

Football Coach.—Don H. O'Donoghue, M.D., was incorrectly identified in the summary report on the Scientific Assembly of the recent A. M. A. convention (The Journal, July 4, p. 1193) as coach of the University of Oklahoma football team. Dr. O'Donoghue, *an orthopedic surgeon, services* the Oklahoma "Sooners" through his clinic in Oklahoma City.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications was June 22. Succeeding examinations—March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23, 1960. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Examination.* Phoenix, Oct. 14-16. *Reciprocity.* Phoenix, Oct. 17. Ex. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

Arkansas:* *Examination and Reciprocity.* Little Rock, Nov. 5-6. Sec., Dr. Joe Verser, Harrisburg.

California: *Written.* Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Connecticut:* *Homepathic. Examination.* Derby, Sept. 8. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

District of Columbia:* *Examination.* Washington, Dec. 14-15. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Florida:* *Examination.* Miami Beach, Nov. 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, Oct. 13. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity.* Kansas City, January 1960. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Louisiana: *Examination and Reciprocity.* New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maryland: *Examination.* Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination and Endorsement.* Boston, July 14-17. Sec., Dr. David W. Wallwork, Room 37, State House, Boston 33.

Montana: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

Nevada:* *Examination and Reciprocity.* Reno, Sept. 8. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

New Hampshire: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

New Jersey: *Examination.* Trenton, Oct. 20-23, *Reciprocity.* Monthly, Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

New Mexico:* *Examination and Reciprocity.* Santa Fe, Nov. 16-17. Sec., Dr. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination.* Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

Ohio: *Examination.* Columbus, Dec. 15-17. *Endorsement.* Columbus, Aug. 26 and Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

Puerto Rico: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Tennessee:* *Examination.* Memphis, Sept. 23-24. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

Texas:* *Examination.* Fort Worth, Dec. 3-5. *Reciprocity.* Houston, Aug. 29-31. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 5. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination and Reciprocity.* Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

Arizona: *Examination.* Tucson, Sept. 15. Sec., Mr. Herman E. Bateman, University of Arizona, Tucson.

Colorado: *Examination.* Denver, Sept. 2-3. *Reciprocity.* Denver, Sept. 4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, Oct. 10. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

District of Columbia: *Examination.* Washington, Nov. 23-24. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Kansas: *Examination.* Pittsburg, Nov. 6-7. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 9-10. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Minnesota: *Examination.* Minneapolis, Oct. 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

Oklahoma: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

South Dakota: *Examination.* Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Texas: *Examination.* Austin, Oct. 12-13. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 11 and Milwaukee, Dec. 5, Sec., Mr. Wm. H. Barber, 621 Ranson St., Milwaukee.

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*Basic Science Certificate required.

DEATHS

Appell, Paul Harry Ⓜ Bristol, Conn.; University and Bellevue Hospital Medical College, New York City, 1923; associated with Bristol Hospital, where he served as secretary-treasurer, vice-president, and president of the medical staff, and chief of the pediatric service; died in Farmington May 20, aged 59.

Bergstein, David Ⓜ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1920; member of the American Academy of General Practice; died while vacationing in Miami Beach, Fla., March 31, aged 64.

Bittner, Linus Herman Ⓜ Glendale, Calif.; University of Oregon Medical School, Portland, 1919; veteran of World War I; formerly a Methodist missionary in Indonesia; served on the staff of the Memorial Hospital of Glendale; died in Acton May 23, aged 69.

Bowman, Lang Fulton Ⓜ Wichita, Kan.; Rush Medical College, Chicago, 1915; served as county coroner; veteran of World War I; died in the Veterans Administration Center May 23, aged 74.

Bridenbaugh, Charles Sumner Ⓜ Emlenton, Pa.; Medical Department of the Western University of Pennsylvania, Pittsburgh, 1903; past-president of the Venango County Medical Society; served as school physician and for many years on the school board; for many years physician for the Selective Service Board; associated with the Franklin (Pa.) Hospital, where he died May 22, aged 79.

Bulkley, Kenneth Ⓜ St. Paul, Minn.; Columbia University College of Physicians and Surgeons, New York City, 1909; service with the Veterans Administration terminated Feb. 19, 1959; died in Glendale April 16, aged 74.

Caplan, Isidor, New York City; Cornell University Medical College, New York City, 1909; died April 13, aged 71.

Carpenter, William Bowers, Sunbury, Ohio; Starling Medical College, Columbus, 1903; died May 23, aged 88.

Christen, Theodore Alphonse, Cincinnati; Universität Bern Medizinische Fakultät, Switzerland, 1894; served as French vice-consul for the Cincinnati area; died May 23, aged 91.

Codington, Herbert Augustus Ⓜ Wilmington, N. C.; University of Maryland School of Medicine, Baltimore, 1911; also a graduate in pharmacy; veteran of World War I; associated with the Community and James Walker Memorial hospitals; died May 21, aged 72.

Cohen, Manley Benjamin Ⓜ El Paso, Texas; Laval University Faculty of Medicine, Quebec, Que., Canada, 1942; interned at the Massachusetts Memorial Hospitals in Boston, where he served a residency; served a residency at the Charlotte Hungerford Hospital in Torrington, Conn.; fellow of the American College of Chest Physicians; member of the American Trudeau Society; veteran of World War II; chief of the medical staff at Providence Memorial Hospital, where he died May 24, aged 44.

Collins, Clarence Bythell, North East, Md.; University of Maryland School of Medicine, Baltimore, 1909; died in Elkton May 29, aged 75.

Cone, William Vernon, Montreal, Que., Canada; born in Conesville, Iowa, May 7, 1897; State University of Iowa College of Medicine, Iowa City, 1922; professor of neurosurgery at the McGill University Faculty of Medicine, where he joined the faculty in 1929; lecturer in neuropathology at his alma mater from 1922 to 1924; from 1926 to 1928 instructor of surgery at Columbia University College of Physicians and Surgeons in New York City; specialist certified by the American Board of Neurological Surgery; member of the American Association for the Study of Trauma, Canadian Medical Association, Harvey Cushing Society, American Neurological Association, American Academy of Neurology, and the Association for Research in Nervous and Mental Diseases; served overseas during World War II and helped organize the No. 1 Neurological Hospital, of which he was appointed chief neurosurgeon with the rank of lieutenant colonel; neurologist and neurosurgeon-in-chief, Royal Victoria Hospital; chief of neurosurgery service at the Montreal Neurological Institute, where he died in his office May 4, aged 61.

Craig, Frank Ardary Ⓜ Philadelphia; born in Philadelphia Sept. 28, 1876; University of Pennsylvania Department of Medicine, Philadelphia, 1898; emeritus professor of clinical medicine at his alma mater and emeritus professor of medicine at the University of Pennsylvania Graduate School of Medicine; veteran of World War I; member of the American Trudeau Society and the American Clinical and Climatological Association; a charter member of the National Tuberculosis Association; last December received the annual award of the Philadelphia Tuberculosis and Health Association "for a life time

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Ⓜ Indicates Member of the American Medical Association.

of outstanding work in tuberculosis control"; first president of the Pennsylvania Trudeau Society and the William B. Lake Foundation; associated with the Phipps Institute of the University of Pennsylvania, where he served as clinical director; served as president and medical director of the White Haven (Pa.) Sanatorium; for many years a member of the visiting staff of the Philadelphia General Hospital, tuberculosis division, and a member of the executive committee of the medical board; consultant in tuberculosis at the Presbyterian Hospital and the Philadelphia General Hospital; author of "Diseases of Middle Life"; died in the Presbyterian Hospital May 11, aged 82.

Crowley, Daniel Francis Ⓜ Des Moines, Iowa; Creighton University School of Medicine, Omaha, 1906; associated with Iowa Lutheran Hospital, Iowa Methodist Hospital, and the Mercy Hospital, where he was once chief of staff, and where he died May 21, aged 81.

Cummings, Frank A. Ⓜ Providence, R. I.; Tufts College Medical School, Boston, 1912; on the courtesy staff of the Rhode Island Hospital, where he was on the active staff from 1919 to 1942; died May 6, aged 75.

Cunningham, Eric Alton Ⓜ Louisiana, Mo.; Washington University School of Medicine, St. Louis, 1926; served as president of the Pike County Medical Society; fellow of the American College of Surgeons; veteran of World War I; chief of staff, Pike County Hospital; member of the board of directors of the Bank of Louisiana; died May 6, aged 60.

Davis, Virgil Allen, New York City; University Medical College of Kansas City, Mo., 1910; died May 22, aged 78.

Dawson, Robert Lee, Bee Branch, Ark. (licensed in Arkansas in 1903); past-president of the Faulkner County Medical Society; died in Little Rock May 22, aged 79.

Dickey, James Lee, Taylor, Texas; Meharry Medical College, Nashville, Tenn., 1921; honored by the city of Taylor as its outstanding citizen of 1952; an engraved plaque given by four local civic clubs went to him; he was especially honored for the good work he had done toward eradicating typhoid fever, tuberculosis, and infant diarrhea among Negroes; died May 18, aged 65.

Dugdale, Allison Harold, Rutherford, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1913; died in New York City April 3, aged 71.

Dyer, Curtis William, Augusta, Maine; Medical School of Maine, Portland, 1918; member of the staff of the Augusta General Hospital; died May 19, aged 65.

Ellenberger, Joseph Mark Ⓜ Norristown, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1912; died in the Montgomery Hospital May 5, aged 76.

Erskine, Gordon McClure Ⓜ Tucson, Ariz.; University of Minnesota Medical School, Minneapolis, 1938; practiced in Grand Rapids, Minn.; died in the Tucson Medical Center May 19, aged 59.

Fehland, Harold Roland Ⓜ Wausau, Wis.; University of Minnesota Medical School, Minneapolis, 1925; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; a vice-regent of the International College of Surgeons; served as chief of the surgical service, St. Mary's Hospital; died in Tomahawk May 6, aged 59.

Ferguson, Georgium Hill, Los Angeles; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1890; died May 5, aged 92.

Fipphen, Earl Edward, Worcester, Mass.; Harvard Medical School, Boston, 1922; fellow of the American College of Surgeons; on the staff of the Worcester City Hospital, where he died May 10, aged 60.

Flynn, Eugene Ⓜ Pierre, S. D.; University of Arkansas School of Medicine, Little Rock, 1933; veteran of World War II; died in St. Mary's Hospital May 2, aged 54.

Fountain, John Horace Ⓜ Captain, U. S. Army, retired, Seattle; born in Washington, D. C., Feb. 16, 1905; Georgetown University School of Medicine, Washington, D. C., 1929; U. S. Army Medical School, 1931; director of the division of tuberculosis control, Seattle–King County Department of Public Health; director of the tuberculosis division, Colorado State Health Department, 1938-1939; served with the California State Department of Health; entered the regular Army in 1930 and retired Sept. 30, 1935; worked for the Washington State Health Department until 1944, when he was named superintendent and medical director of the Morningside Tuberculosis Hospital, remaining there until 1946; specialist certified by the American Board of Preventive Medicine; member of the American Trudeau Society and the American Public Health Association; clinical instructor in public health and preventive medicine, University of Washington School of Medicine; died May 1, aged 54.

French, Joel Erle, Memphis, Tenn.; Memphis (Tenn.) Hospital Medical College, 1908; on the staff of Baptist Memorial Hospital; died May 4, aged 81.

Fuerth, Arthur Laurence Ⓜ Cape Girardeau, Mo.; St. Louis University School of Medicine, 1916; fellow of the American College of Surgeons; veteran of World War I; at one time associated with the St. Louis City Hospital; associated with St. Francis Hospital, where he died May 2, aged 66.

Gittinger, William Carl Ⓜ Brooklyn; born in New York City June 24, 1926; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1949; member of the New York Heart Association and the American Geriatrics Society; certified by the National Board of Medical Examiners; served as instructor in physiology, bacteriology, and medicine, assistant to the dean, New York Medical College, Flower and Fifth Avenue Hospitals, and instructor in medicine at the Yale University School of Medicine, in New Haven, Conn.; veteran of World War II; served as industrial medical officer at Boston Naval shipyard during the Korean War; medical director of Pfizer Laboratories division, Charles Pfizer & Company, Inc., New York City; died in Chase, Baltimore County, Md., May 12, aged 32.

Godbey, John Campbell Jr. Ⓜ Morenci, Ariz.; Southwestern Medical School of the University of Texas, Dallas, 1944; veteran of World War II; interned at Baylor University Hospital in Dallas, Texas, where he served a residency; formerly associated with the Johns Hospital in Taylor, Texas; on the staff of the Morenci Hospital; died May 7, aged 44.

Gosling, John Anthony Ⓜ Tiffin, Ohio; Rush Medical College, Chicago, 1901; veteran of World War I; for many years city health commissioner; surgeon for the New York Central Railway; on the staff of the Mercy Hospital, where he died May 8, aged 85.

Hampton, Henry Hunton Ⓜ Chattanooga, Tenn.; Johns Hopkins University School of Medicine, Baltimore, 1914; fellow of the American College of Surgeons; served as chief of staff at Mount Sinai Hospital in Baltimore; associated with Erlanger and T. C. Thompson Children's hospitals; a director of the Pioneer Bank; died May 8, aged 76.

Hartman, John Chilton, Campbellsburg, Ky.; University of Louisville Medical Department, 1908; died in the King's Daughters' Hospital, Shelbyville, May 4, aged 74.

High, Clifton Earle Ⓜ Pampa, Texas; Baylor University College of Medicine, Dallas, 1924; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; veteran of World War I; associated with the Highland General and Worley hospitals; died May 10, aged 59.

Hobbs, Armenious Clements Jr. Ⓜ Columbus, Ga.; born in Cataula, Ga., Jan. 27, 1920; University of Georgia School of Medicine, Augusta, 1946; served an internship at the Columbus City Hospital in Columbus, Ga., and a residency at Jefferson–Hillman Hospital in Birmingham, Ala.; specialist certified by the American Board of Ophthalmology; fellow of the American Academy of Ophthalmology and Otolaryngology; captain in the medical reserve corps of the U. S. Army, 1948-1949; on the staffs of St. Francis Hospital and Medical Center; consultant, Station Hospital in Fort Benning, Ga., and the Veterans Administration Hospital in Tuskegee, Ala.; served as secretary-treasurer of the Muscogee County Medical Society; an associate editor of the *Bulletin of the Muscogee County Medical Society;* president of the Columbus Philharmonic Guild; died May 8, aged 39.

Hockett, Lester Emlen Ⓜ Vancouver, Wash.; North Carolina Medical College, Charlotte, 1917; past-president of the Clark County Medical Society; received a citation and Congressional Medal of Merit for services rendered on the Selective Service Board during World War II and an award from the Governor for services on the Selective Service Board; past-president of the staffs of St. Joseph and Vancouver Memorial hospitals; chief surgeon of the Washington State School of the Deaf; died May 16, aged 68.

Hoy, Carl Da Costa, Columbus, Ohio; Northwestern University Medical School, Chicago, 1907; for many years associated with the White Cross Hospital; veteran of World War I; died May 5, aged 76.

Ireland, R. Lindsey Ⓜ Louisville, Ky.; Kentucky School of Medicine, Louisville, 1894; Louisville (Ky.) Medical College, 1894; for many years on the medical staffs of Norton Memorial Infirmary and Kentucky Baptist Hospital; staff physician for Southern Baptist Theological Seminary; chief of medical staff, Spring Meadows, Baptist orphanage at Middletown; died May 8, aged 86.

Jordan, George Thomas, Vermillion, S. D.; born in Vermillion, May 17, 1876; Rush Medical College, Chicago, 1905; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; professor of otolaryngology and ophthalmology at the University of South Dakota School of Medical Sciences and in 1957 was presented a distinguished service award at its annual banquet in recognition of his many years of service devoted to clinical instruction in the field of otolaryngology and ophthalmology; formerly practiced in Chicago, where he was on the faculty of Loyola University School of Medicine and on the staff of the Mercy Hospital; veteran of World War I; chief of staff at the Dakota Hospital; died May 17, aged 83.

Kilgore, Alson Raphael Ⓜ Belvedere, Calif.; born in Oakland, Calif., May 30, 1887; Harvard Medical School, Boston, 1914; member of the founders group of the American Board of Surgery; member of the American Surgical Association; fellow of the American College of Surgeons; past-president of the Pacific Coast Surgical Association, San Francisco Surgical Society, and the San Francisco Medical Society; veteran of World War I; served on the faculty of the University of California School of Medicine in San Francisco; until 1918 taught at the Harvard Medical School in Shanghai, China; first secretary-treasurer of the California Physicians' Service, of which he was a founder and an original trustee; chief surgeon for the Western Pacific Railroad for 25 years; associated with the Chinese Hospital; for many years chief of surgery at Children's Hospital and chief of staff at St. Joseph's Hospital in San Francisco, where he died May 20, aged 71.

Lee, Willard Judd, Garden City, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1923; served during World War I; veteran of World War II and was awarded a commendation citation; served on the staffs of the Nassau Hospital in Mineola, Mercy Hospital, Rockville Centre, and South Nassau Communities Hospital in Oceanside; formerly surgeon of the city fire department; died in the Memorial Hospital, New York City, May 11, aged 61.

Liepmann, Hans Walter Ⓜ Central Valley, N. Y.; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1925; school physician for the Monroe-Woodbury Central School District; on the staffs of the Goshen (N. Y.) Hospital, St. Luke's Hospital, Newburgh, and Cornwall (N. Y.) Hospital; died May 6, aged 56.

Linde, Herman Ⓜ Cyrus, Minn.; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1905; died at the Stevens County Memorial Hospital in Morris May 10, aged 87.

McBain, Louis Bernard Ⓜ Appleton, Wis.; University of Wisconsin Medical School, Madison, 1930; veteran of World War II; member of the American Academy of General Practice; a member of St. Elizabeth's Hospital; died May 3, aged 53.

McKinney, Edgar Prentice Ⓜ Nacogdoches, Texas; University of Virginia Department of Medicine, Charlottesville, 1933; veteran of World War II; died in the Hermann Hospital, Houston, May 6, aged 51.

McKinney, Thomas Seldon Ⓜ born in Moonachie, N. J., Nov. 14, 1918; Maywood, N. J.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1944; certified by the National Board of Medical Examiners; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists; veteran of World War II; served in Korea in 1953-1954; assistant director of the department of anesthesiology at Hackensack (N. J.) Hospital, where he died May 4, aged 40.

McLeod, Donald Norman Ⓜ Tucson, Ariz.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1948; member of the American Academy of General Practice; associated with St. Mary's Hospital and the Tucson Medical Center, where he died May 5, aged 33.

Marks, Jacob Keene Ⓜ Philadelphia; Temple University School of Medicine, Philadelphia, 1914; veteran of World War I; for many years on the staff of the Stetson Hospital, where he died May 17, aged 66.

Meyer, Hugh Raymond Ⓜ Lansing, Mich.; University of Michigan Medical School, Ann Arbor, 1917; died May 5, aged 68.

Murphy, Harry E. Ⓜ Franklin, Ind.; born in Morgantown, Ind., Sept. 16, 1894; Indiana University School of Medicine, Indianapolis, 1918; past-president of the Johnson County Medical Society; member of the American Academy of General Practice; veteran of World War I; health officer of Johnson County; from 1945 to 1952 served as the Seventh District Republican chairman; on the staffs of Methodist Hospital, Indianapolis, and the Johnson County Memorial Hospital; died in St. Mary's Hospital, Rochester, Minn., May 8, aged 64.

Myers, John Llewellyn Ⓜ Des Moines, Wash.; born in Bedford, Mo., March 29, 1872; College of Physicians and Surgeons, Medical Department of the Kansas City University, Kansas City, Kan., 1904; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and for many years secretary of the section on otology, rhinology and laryngology; member of the American Laryngological Association and the American Association for the Advancement of Science; fellow of the American College of Surgeons; vice-chairman, Section on Laryngology, Otology and Rhinology of the American Medical Association, 1932-1933; in 1941 was presented a gold medal by the Kansas City (Mo.) Society of Ophthalmology and Otology, of which he was president in 1921, as a mark of appreciation of his work in the society; in 1931 president of the Kansas City Southwest Clinical Society; formerly on the staffs of the University of Kansas Medical Center, Kansas City, Kan., and Research and St. Mary's hospitals in Kansas City, Mo.; served as associate professor of otorhinolaryngology at the University of Kansas School of Medicine, Kansas City, Kan.; first president of the Alaska Board of Medical Examiners, of which he was an organizer; for many years practiced in

Ketchikan, Alaska, and served as a medical missionary; veteran of World War I; died May 20, aged 87.

Neraal, Paul O. ⓜ Cut Bank, Mont.; State University of Iowa College of Medicine, Iowa City, 1897; health officer of Glacier County from 1921 to 1956; served as county coroner and as physician for the Great Northern Railway; past-president of the North Central District Medical Association; associated with the Glacier County Memorial Hospital; died May 9, aged 88.

Northrop, David Daniel ⓜ Lansdale, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1931; veteran of World War II; regional medical director of Multiple Sclerosis Foundation; associated with Grand View Hospital in Sellersville and medical director of the North Penn Hospital, where he died May 24, aged 54.

Oates, Louis Thomas, Morrilton, Ark.; University of Arkansas School of Medicine, Little Rock, 1905; one of the organizers of the First State Bank of Morrilton, where he was vice-president and chairman of the board of directors; died May 2, aged 83.

Parker, Joseph B. ⓜ Knoxville, Tenn.; Tennessee Medical College, Knoxville, 1895; University of Louisville (Ky.) Medical Department, 1897; served as county physician for three years; elected to the office of register of deeds from 1932-1940; associated with the Fort Saunders Presbyterian Hospital; died May 13, aged 89.

Pensig, Arnold Walter ⓜ Brooklyn; born in Brooklyn Feb. 12, 1926; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1948; interned at the Jewish Hospital in Brooklyn and the Bellevue Hospital in New York City; served a residency at the Goldwater Memorial Hospital in New York City and the Maimonides Hospital in Brooklyn; clinical assistant, medicine, State University of New York College of Medicine at New York City; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; member of the American Association for the Advancement of Science; a director of the Brooklyn Tuberculosis and Health Association; on the staffs at Maimonides and Kings County hospitals; associate medical director of Pfizer Laboratories division, Charles Pfizer & Company, Inc., New York City; served in the U. S. Public Health Service Reserve as medical officer at the U. S. Coast Guard Academy in New London, Conn., from 1956 to 1958; died near Baltimore May 13, aged 33.

Perkins, Joseph Ashbridge ⓜ West Chester, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1916; retired in 1957 as chief plant physician at Lukens Steel Company; on the staff of the Coatesville (Pa.) Hospital, where he died May 13, aged 67.

Postelle, Joseph McDowell ⓜ Houston, Texas; Baltimore Medical College, 1894; veteran of World War I; died May 14, aged 94.

Reagan, Rezin ⓜ Sioux Falls, S. D.; born in Sheridan, Ind., Nov. 8, 1882; Rush Medical College, Chicago, 1913; member of the American Academy of General Practice; past-president of the Seventh District Medical Society; served in France during World War I; formerly medical member of the claims rating board of the Veterans Administration regional office from 1954 to 1957; associated with McKennan and Sioux Valley hospitals; for many years medical director of the National Reserve Life Insurance Company; died May 10, aged 76.

Rowley, Robert Lee ⓜ Hartford, Conn.; Yale University School of Medicine, New Haven, 1903; retired in 1950 as medical director of the Phoenix Mutual Life Insurance Company; past-president of the Association of Life Insurance Medical Directors of America; for many years on the state medical examining board; associated with the Hartford Hospital, where he was a member of the board of directors from 1928 to 1958, and where he died May 5, aged 79.

Rund, Emmet Henry ⓜ St. Louis; National University of Arts and Sciences Medical Department, St. Louis, 1918; fellow of the American College of Surgeons; instructor in gynecology and obstetrics at St. Louis University School of Medicine; on the staff of St. Mary's Group of Hospitals, Alexian Brothers Hospital, Incarnate Word Hospital, Firmin Desloge Hospital, and St. Anthony's Hospital; associated with St. Louis City Hospital from 1930 to 1935; from 1933 to 1941 surgeon for the police department; died in St. Anthony Hospital May 19, aged 67.

Schatanoff, Louis ⓜ New Freedom, Pa.; Long Island College Hospital, Brooklyn, 1927; on the staff of the York Hospital; died May 7, aged 57.

Scheidell, Dorothy Katherine ⓜ Quincy, Mass.; Cornell University Medical College, New York City, 1932; fellow of the American College of Surgeons; associated with the Quincy City Hospital; on the staffs of the Faulkner and New England hospitals in Boston; died in the Massachusetts General Hospital in Boston May 5, aged 51.

Tupker, Eugene Powers ⓜ St. Helens, Ore.; Creighton University School of Medicine, Omaha, 1932; veteran of World War II; served on the staff of the Oregon State Hospital in Salem; died May 8, aged 52.

FOREIGN LETTERS

BRAZIL

Metaplasia of Gastric Mucosa.—According to Dr. Jorge Michalany (*Revista da Associação medica brasileira,* February, 1959) intestinal metaplasia represents the epithelial lesion of chronic gastritis and it may interfere with gastric secretion. The increased secretion of serotonin by argentaffin cells, which are increased in intestinal metaplasia, may cause hyperperistalsis. Intestinal metaplasia of the gastric mucosa is not necessarily precancerous, despite some reports to the contrary. The enteroid structure in most cases of gastric carcinoma depends, principally, on the metaplastic capacity of the neoplastic cells themselves.

Intervertebral Disks.—Dr. Rolando Tenuto analyzed a series of 128 patients operated on for herniated lumbar intervertebral disks. These patients had been carefully observed for at least one year (*Arquivos de neuro-psiquiatria São Paulo,* March, 1959). Good results, i. e., no remaining signs or symptoms, were obtained in 78.2%, improvement in 10.9%; and no relief in 10.9%. Operation is indicated in patients with this condition when (1) conservative treatment is ineffective, (2) sensory or motor deficits are evident, and (3) acute damage of several nerve roots is present. Myelography should always be added to the clinical examination, since it will localize the lesion.

GERMANY

Cerebral Tuberculomas.—Within seven years four cerebral tuberculomas were observed by W. Jacoby (*München. med. Wchnsch.* 101:890, 1959). In each case the diagnosis was made by histological examination of the resected lesion. In two patients the tuberculomas were found in the cerebral hemispheres, and in two others they were found in the posterior cranial fossa. Three patients recovered after operation and were cured. One patient died during the operation but would have died anyway because of the wide extent of the tuberculoma. Postoperative tuberculous meningitis, formerly a common and dreaded complication, can now be prevented by the use of streptomycin.

Anomalies in Newborn Infants After Estrogenic Treatment of Mothers.—Three cases of multiple gross developmental disorders were observed in newborn infants whose mothers had been treated with large doses of estrogens in the early stages of pregnancy. These were reported by H. Uhlig (*Geburtshilfe und Frauenheilkunde,* vol. 19, 1959). Estrogens had been given to two to induce abortion. The malformations involved the brain and spinal cord (hydrocephalus, meningomyelocele, and rachischisis), lungs, liver, spleen, intestine, muscles, and bones. Embryogenic considerations indicated that abnormal fetal development began synchronously with estrogen treatment. The assumption of a causal relationship between the latter and the observed developmental disorders was, therefore, justified. Experiments in pregnant rats, showing severe fetal damage after the administration of estrogens, support this view.

Carcinoma of the Ovaries.—The method used at the gynecologic clinic of the University of Heidelberg for the treatment of carcinoma of the ovaries was described in detail by Buttenberg and Lau (*Geburtsh. u. Frauenh.* 19:323, 1959). Treatment consists of (1) excision of both ovaries without removal of the uterus, or, if this proves impossible, removal of the bulk of the tumor masses, no attempt being made to radically eradicate all carcinomatous tissue; (2) repeated intra-abdominal instillation of 120 mc. of colloidal radioactive gold, the first being given immediately after the operation; (3) intrauterine application of radioactive cobalt (the maximum dose delivered to the bladder and rectum being 4,000 r), either deep x-ray therapy with one field each over the abdomen and the back with a surface dose of 6,000 r or telecobalt therapy with doses of 4,000 to 5,000 r is used; and (4) continuous therapy with large doses of androgens in combination with prednisone. With this treatment the survival time of 24 patients with incurable cancer of the ovaries could be prolonged by an average of three months, compared with a group of 29 similar patients treated during the period 1945-1950. In view of the unfavorable prognosis of carcinoma of the ovaries this prolongation of survival time, although small, is of some value, particularly as the patients regain a feeling of well-being. The use of cytostatic agents is rejected because of the additional risk of damage to the leukopoietic system, but hypophysectomy is advocated as a supplementary measure to hormone treatment.

Hyaline Membranes in Premature Infants.—Hyaline membranes are found primarily in premature infants and represent an exudation of blood con-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

stituents in septums and alveoli of the lungs. Because of insufficient reabsorption these are condensed and cause a membranous strangulation of the peripheral respiratory passages. According to Braun and Mann (*Arch. Kinderh.* 159:130, 1959) these membranes may contain cellular materials, decomposition products, and lipid droplets. The blockade of the gas exchange converts the temporary anoxia of premature infants into a manifest anoxia and causes death. As with infants suffering from asphyxia neonatorum these infants have dyspnea, cyanosis, and occasionally attacks of apnea also. There is no effective treatment.

Neonatal Liver Function.—A series of liver function tests were performed during the first 10 days of life to evaluate the functional capacity of the liver in mature and immature newborn infants by Dieckhoff and Schmidt (*Arch. Kinderh.* 159:113, 1959). Particular attention was given to the intravenous levulose tolerance test. This test, when showing pathological values, confirmed the results of the serum bilirubin determination, the sulfobromophthalein test, and the electrophoretic pattern of the serum during the same period of life. The reduced capacity of the liver of the newborn, interpreted as functional immaturity, was shown by the following results, premature babies showing weaker function than full-term infants.

In premature infants serum bilirubin concentration was at all times higher than in full-term infants. Most of the total bilirubin consisted of indirect-reacting bilirubin. In 35% of the infants examined the presence of direct-reacting bilirubin could be shown. The retention of sulfobromophthalein in the blood decreased with increased age but did not depend on the birth weight. When correlated with the simultaneous bilirubin level there appeared to be a coexisting disturbance of two partial functions. In premature infants serum electrophoresis revealed an increase of the albumin fraction with lowered values for the globulins, and hypoproteinemia was more marked than in full-term infants. When comparing full-term and premature babies with older infants there was a definite reduction in the breakdown of levulose after intravenous loading. Particularly 20 to 60 minutes after injections the levulose concentration in the blood of immature newborn infants was above normal.

Antibiotic-Resistant Staphylococci.—L. Grün of Düsseldorf (*Die Medizinische*, no. 4, p. 143, 1959) stated that in addition to the problem of the development of antibiotic-resistant (AR) staphylococcic strains in hospitals there is the problem of the transmission of AR to the general public by healthy carriers. Some of these strains may cause small epidemics. Staphylococcic respiratory diseases are clearly on the increase. In many cases an infection with an AR strain becomes manifest only after discharge from hospital. The importance of pathogen-carrying hospital personnel who contribute to the spread of epidemic strains is recognized. Whether infection is transmitted through the air or by contact has not been determined, but it appears likely that both these modes are operative. Ultraviolet irradiation of the air in the operating room greatly reduces bacterial contamination. Another helpful measure is an increase in the air circulation. Although the elimination of all carriers of the infection is not possible the rate of infection can be lowered by ultraviolet irradiation, spraying with triethylene glycol, and disinfection of linen. Beds should be made of latex foam, which is bactericidal in itself.

Streptococcic Infections.—W. Schmid of Würzburg (*Med. klin.* 54:296, 1959) studied serums from 60 patients for antistreptolysin and C-reactive protein levels. In 16 patients (4 who had rheumatic polyarthritis with cardiac involvement, 9 who had endocarditis with acute rheumatic polyarthritis, and 3 who had septic fever of unknown origin) the two reactions were parallel. In the others (those with acute nephritis, rheumatoid arthritis, and rheumatic manifestations without cardiac involvement) only the antistreptolysin values were elevated. It was concluded that the antistreptolysin levels were a more reliable criterion of the activity of inflammatory rheumatic diseases than the demonstration of C-reactive protein, although the latter also tends to decline in response to adrenocortical hormone therapy. The principal difference was that antistreptolysin develops only after immunization with streptolysin O, which is produced by beta hemolytic streptococci, while C-reactive protein may occur in diseases of various origins.

Circumscribed Opacities in the Lung.—F. Lindner of Berlin (*München. med. Wchnschr.* 101:787, 1959) studied a series of circumscribed opacities in the lung and found that 31.9% were carcinoma, metastases, or sarcoma; 14.6% were benign tumors (hamartoma, chondroma, bronchial adenoma, mesothelioma, neurofibroma, or hemangioma); and 53.5% were caused by inflammatory changes (tuberculosis, chronic pneumonic foci, cysts, pulmonary abscesses, pneumomycoses, or parasites such as Echinococcus). In most cases a clearcut diagnosis could be obtained only by thoracotomy. Differential diagnosis by radiology was inconclusive, even when it gave some indications of form, localization, and structure. Rapid growth indicated sarcoma. In advanced age carcinoma might also be suspected. All diagnostic aids should be used in the diagnosis of circumscribed tumors. Since the operative death rate associated with the removal of circumscribed tumors is low, surgical removal should always be resorted to.

Postoperative Hepatic and Renal Complications.—H. E. Bock of Marburg (*München. med. Wchnschr.* 101:785, 1959) stated that hepatic complications (19 of these hepatorenal) occurred after 119 of 6,000 major operations and caused 60 deaths. Postoperative renal damage was much more frequent. Operation in the presence of renal damage is associated with a major risk. Of 139 patients with an elevated nonprotein nitrogen level who were operated on 70 died. Nonprotein nitrogen and creatinine level determinations should always be made prior to operation. The urea clearance test is recommended only if the creatinine level exceeds 1 mg.%. If hepatic damage is suspected, the author recommended withdrawal of proteins, anticoagulants, mixed infusions (levulose, electrolytes, and metabolites), and prednisolone, and avoidance of the use of the duodenal tube for aspiration and feeding. To bridge the prolonged stage of anuria, hemodialysis is the only effective treatment. No disease should be judged from the laboratory findings alone, however important they may be, but all clinical findings should be considered.

Postoperative Infusions of Electrolytes.—H. Herken of Berlin (*München. med. Wchnschr.* 101:785, 1959) stated that in health the delicate electrolyte regulatory system keeps the water and salt content constant within a comparatively narrow range. The antidiuretic pituitary hormone and certain corticosteroids (especially aldosterone from the adrenals) have a major share in these regulatory processes. Because of postoperative changes in the production of adrenocortical hormone marked retention of sodium and an increase of the excretion of potassium occur. If secretion of urine is restricted, extrarenal losses of fluid (insensible perspiration) lead to the accumulation of sodium chloride. The postoperative regulatory disturbance is reversible. Infusions of electrolyte solutions are merely intended to compensate for postoperative fluid losses and to maintain diuresis. If the daily amount of urine is 600 cc., and the water loss with the stool about 200 cc., the quantity lost by perspiration is to be calculated as 1,000 cc. Thus, it is necessary to replenish 1,800 cc. of fluid. To prevent the retention of substances likely to be excreted with the urine a daily minimum of 500 to 600 cc. of urine is required. Morphine, hexobarbital, and chlorpromazine impair diuresis. Since hormones are unsuccessful in preventing electrolyte disturbances, the clinician should wait for spontaneous remissions.

Parenteral Feeding.—O. Lindenschmidt of Hamburg (*München. med. Wchnschr.* 101:786, 1959) stressed the importance of parenteral nutrition in the postoperative period until fluids can be taken by mouth. Entirely parenteral feeding should not be extended any longer than necessary and never beyond three or four days after the operation. If necessary tube feeding may be used. To prevent postoperative disorders it is necessary to compensate for any preoperative deficit in proteins. Careful preparation for operation is more important, more reliable, and less complicated than postoperative substitution by infusions. Preoperative protein loss can best be compensated by administration of whole blood or plasma and human albumin. Preoperative administration of amino acid mixtures is not very suitable; 30% is excreted and of the other 70% most is decomposed, so that little remans available for the synthesis of albumin. Plasma and human albumin do not need calories to be split. Postoperative energy supply is best provided by dextrose or levulose infusions. The administration of 200 to 250 cc. of whole blood, plasma, or human albumin is also recommended. Only in the late phase, when special importance is attached to protein-rich nutrition, is the administration of amino acid mixtures a suitable supplement. Indiscriminate infusion is dangerous. Clinical observations (thirst, moisture of skin and mucosa, nausea, and dizziness) should always be considered, apart from laboratory findings. Also, an excess of infusions and transfusions is dangerous.

Tuberculous Osteitis.—K. Treppinger (*Ztschr. Tuberk.-Arzt.* 13:106, 1959) reported on a series of 213 patients with tuberculous osteitis who received, in addition to the usual treatment, 3 to 5 mg. of isoniazid per kilogram of body weight. He concluded that therapy with isoniazid does not directly shorten the course of the disease, but it quickly brings the patient to a stage in which he can be operated on. The prospects for lasting ability to work were greater in these patients the longer the period of isoniazid administration had been. The incidence of relapses and flare-ups of new foci also diminished proportionately with the length of this treatment.

Isoniazid Therapy.—G. Bahrs (*Ztschr. Tuberk.-Arzt.* 13:157, 1959) made follow-up examinations of 200 patients who had received 10 mg of isoniazid per kilogram of body weight daily. About 33% of the patients had been pretreated with vitamin D or amithiozone. Of 159 patients with skin tuberculosis so treated 114 or 71% and of 119 patients with lupus vulgaris 76 or 64% remained cured. With a total dosage of 120 to 200 Gm. of isoniazid only three patients were not primarily cured. Of 24 patients with tuberculosis cutis indurativa cure persisted in 14 and failed in 6. Patients with mucosal lupus erythematosus responded well to isoniazid as did those with tuberculosis cutis verrucosa. There was no failure and no relapse in six patients treated with 40 to 60 Gm. of isoniazid. Patients with tuberculosis of the lymph nodes and tuberculosis cutis colliquativa responded less well and those with papulonecrotic tuberculides poorly. Long-term treatment with isoniazid alone, which is successful in dermal tuberculosis, is now rarely used in pulmonary tuberculosis. Therefore, it is not yet possible to evaluate this form of treatment in pulmonary tuberculosis. While para-aminosalicylic acid has completely failed in dermal tuberculosis, streptomycin is effective.

INDIA

Concentration Methods for Intestinal Parasites.—P. T. Acharya and co-workers (*Journal of the Indian Medical Association*, vol. 32, April 16, 1959) compared four methods of detecting protozoal cysts and helminthic ova in 400 samples of feces. The methods used were (1) direct examination of a wet preparation, (2) acid-ether concentration, (3) zinc sulfate concentration, and (4) brine flotation. Direct examination of a wet preparation was superior to the acid-ether method, except for the detection of cysts of Entameba coli. In the latter method the cysts became distorted and unrecognizable. The zinc sulfate method was superior to both the above techniques. The brine flotation method gave disappointing results, especially for the detection of Giardia lamblia cysts. Cysts were detected in 18 samples by direct examination when they were missed by all the other techniques. This method should therefore always be used with the zinc sulfate concentration technique. The acid-ether method was more useful than direct examination for detecting hookworm ova. For detecting ova of Ascaris lumbricoides, Trichuris trichiura, and Enterobius vermicularis, the acid-ether method did not give better results, and for ova of Hymenolepis nana direct examination gave much better results. The zinc sulfate method proved much more useful than both these methods for helminthic ova also. The brine flotation technique was even better, the best results being obtained by brine flotation along with the direct examination. Thus for protozoal cysts the zinc sulfate concentration method was most efficient, and for helminthic ova the brine flotation technique gave the best results.

JAPAN

Narcotics Problem.—The Bureau of Health and Welfare reported that crime waves related to narcotics addiction are on the increase. The number of arrests for violations of narcotics laws in 1952 was 982 and in 1958 was 1,767. As in the United States unwise narcotics laws have forced addicts to become peddlers of drugs from illegal sources. About 25% of the offenders are women. The government abolished legalized prostitution, but, since no funds were provided for the rehabilitation of these girls, many have turned to peddling narcotics. Of those arrested 68% were themselves addicts.

NORWAY

Alkaline Phosphatase and Iron in Jaundice.—J. S. Bødtker (*J. Oslo City Hosp.* 9:62-71 [March] 1959) studied the serum alkaline phosphatase and serum iron levels to determine their value in the differential diagnosis of jaundice. His series of 128 patients consisted of all patients over 20 years of age admitted between 1953 and 1957 to the Aker Hospital with a diagnosis of acute or chronic hepatitis, cirrhosis of the liver, stone in the common bile duct, cancer of the liver, cancer of the gallbladder, cancer of the pancreas, or jaundice; 12 patients with cholecystitis and cholelithiasis were included for the purpose of comparison with the group that had cholelithiasis alone. Increased values were found in all those with extrahepatic or intrahepatic obstructive jaundice. Alkaline phosphatase levels provided no clue to a differentiation between extrahepatic obstructive jaundice and primary intrahepatic cholestasis. Moderately increased phosphatase values were generally encountered during the initial phase in those with acute hepatitis but occasionally also in other groups with more complicated findings, probably indicating a phase of intrahepatic cholestasis.

A correlation between serum alkaline phosphatase and iron levels and icterus index could not be demonstrated. Acute hepatitis in early stages was associated with an increase in serum iron level in about 75% of the patients. In those with cirrhosis of the liver and chronic hepatitis high normal values were usually encountered, while low normal values were noted in those with obstructive jaundice due to calculi or malignant tumor, and in those with cholecystitis and cholelithiasis. Patients with drug-induced intrahepatic cholestasis had normal values. Serum iron estimations might be useful in the differentiation between intrahepatic and extrahepatic cholestasis.

SWEDEN

Precancerosis of the Penis.—Edsmyr and Ekström (*Acta chir. scandinav.* 116:296-305, 1958/1959) described precancerosis of the penis as an exophytic papillomatous lesion of the glans and prepuce which in histological examination shows no definite infiltrative growth. Compared with penile cancer it is fairly uncommon. The present series comprised 25 patients, of whom 15 had phimosis. Nine had had the condition since childhood and the other 6 had had surgical treatment for phimosis 5 to 30 years before the precancerous lesions were observed. The age distribution was similar to that in patients with cancer of the penis, but the mean age was somewhat lower. Phimosis seemed to have the same etiological significance as in cancer of the penis. Venereal disease was not an important factor in causing precancerosis, nor is it in patients with cancer. The macroscopic appearance of precancerosis does not usually differ from that of the papillary form of penile cancer, although the local extent of precancerosis is often greater.

Biopsy specimens from penile tumors seemed almost always to permit reliable histological diagnosis and to be representative of the tumor in question. In none of the authors' series did precancerosis of the penis give rise to inguinal metastases or undergo changes to infiltrative cancer. A trial of conservative therapy, reserving amputation for unsatisfactory results, would thus seem to imply no risk. Because the series was small the authors believed that it allowed no reliable comparative evaluation of different types of conservative treatment. Radiotherapy probably was the most effective and most suitable measure and appeared to be preferable to electrocoagulation. Only if precancerosis was confined to the prepuce was local excision (circumcision) justified. Of 18 conservatively treated patients 4 later underwent amputation. In three the indication was recurrence of the growth and in the fourth amputation was performed for irradiation necrosis 10 years after radiotherapy was begun. The other 14 patients showed no recurrence. Ten of them were followed up for 4 to 14 years and four for shorter periods. The results of conservative therapy were also good from the functional aspect. In no case did the treatment cause impotence. Twelve of the patients received prophylactic treatment consisting of telegamma rays in fractionated dosage, totaling 3,000 to 4,500 r to each of two fields in either groin (the same dosage as in cancer of the penis), and the other 13 patients had no inguinal irradiation. The authors concluded that irradiation of the inguinal lymph nodes in precancerosis is superfluous.

Scandinavian Hospital in Seoul.—Up to March 31 the Scandinavian teaching hospital in Seoul, Korea (opened in November, 1958), had treated 878 inpatients, and the outpatient department had had 7,100 visits from 3,801 registered patients. There are 90 Scandinavians on the hospital staff. Qualified assistant Korean staff members are still hard to find.

Artificial Nose.—An artificial nose was designed by Prof. Hjalmar Koch and co-workers. The apparatus, which takes over the function of the nose by giving the inhaled air body temperature and saturating it with moisture, is of great value to patients on whom it has been necessary to perform a tracheotomy. Formerly, tracheotomy was performed mainly as a lifesaving operation in patients with inflammation of the trachea, false croup, and true croup, but the circumstances changed radically during the severe poliomyelitis epidemics in the 1940's and 1950's. At the meeting of the Swedish Otolaryngological Society in Lund in May Prof. Koch stated that poliomyelitis also caused paralysis of the muscles of the pharynx and trachea. These patients lost the power to get rid of the secretions which run from nose and throat into the lungs and thus they drown in their own secretions. The respirator does not adequately serve its purpose, since the prime necessity is to keep the air passages free from obstruction. The artificial nose has helped to solve this problem.

UNITED KINGDOM

Penicillin-Resistant Staphylococci.—The rising incidence of penicillin-resistant strains of Staphylococcus aureus in hospitals is due to a real increase in penicillin resistance and to cross-infection in the wards. Little information, however, is available on the incidence of resistant strains in the general population. To obtain an indication of this Buhr and Scott studied strains isolated from hospital outpatients with hand infections (*Lancet* 1:1019, 1959). These were chosen because in the same unit six years ago these workers noted that of 82 hand infections due to Staph. aureus no penicillin-resistant strain was found. Swabs were taken from 290 patients treated in the accident service of the united Oxford hospitals. Of these 267 patients were from the general public and 23 were doctors, nurses, hospital personnel, or hospital staphylococcus contacts. Of the swabs from infected lesions of these 23, penicillin-resistant staphylococci were found in 16 (68%) in contrast to 30% of those from lesions in patients from the population at large. Of the penicillin-resistant organisms in the hospital staff 6 or 29% were also resistant to chlortetracycline. In nurses the percentage of penicillin-resistant strains of staphylococci reached 97%. Of 187 outpatients from the general population who had not had penicillin therapy for the hand infection under review 27% had penicillin-resistant strains of Staph. aureus, compared with 37% of those who had received penicillin some time previously.

The data confirm not only the high incidence of penicillin resistance among hospital staff, particularly nurses, but also among the general population, which has increased from 0 to 30% in the Oxford area within six years. The authors pointed out that, with hospital staphylococci so often resistant to penicillin, all available methods should be used to reduce hospital infection. The introduction of antibiotics has increased, not decreased, the need for aseptic and antiseptic vigilance.

The Church and Medicine.—Writing in the *Canterbury Diocesan Notes* the Archbishop of Canterbury said that there has always been a natural and inevitable affinity between the church and the medical profession, since their ministries of healing cannot be separated, but it had come to appear to many people that in their partnership the one was scientific and authoritative and the other sentimental and subsidiary. There is in many quarters a renewed sympathy between the two and a recognition that in many ways neither can do the perfect work of healing without the cooperation of the other. On neither side of the partnership is there infallibility. Neither can dictate to the other, but in their joint pursuit of spiritual and physical health they need each other. This is especially so when they deal from either side with questions that are moral as much as or more than medical. A physician is perfectly free to publish an article disagreeing with the church's view of fornication or other moral aberrations, but great injury to both sides of the partnership results, unless he makes it clear that he does not speak for his profession and that the fact of his being a doctor does not give him any special competence to deliver judgment on moral questions. It is always a serious matter to take the law, moral or civil, into one's own hands.

Effect of New Steroid on Synovial Fluid.—Few studies have been made of the biochemical and cytological changes occurring in synovial fluid after the intra-articular injection of steroids. Murdoch and Will (*Brit. M. J.* 1:1271, 1959) injected a new steroid, prednisolone trimethylacetate, into joint spaces. This drug is said to have a lower solubility than hydrocortisone and to remain in the synovial fluid longer. A clinical appraisal was first made of the effect of giving this new steroid intra-articularly to 35 patients with rheumatoid arthritis, osteoarthritis, and recurrent hydrarthrosis; 20 mg. of a microcrystalline suspension was injected into the knee joint. The effectiveness of treatment was measured by reduction in size of the swollen joint and by relief of pain. From 2 to 12 injections were given at intervals of one week. In the group with rheumatoid arthritis the results were good in 85.0%, fair in 7.5%, and poor in 7.5%. Only six patients with osteoarthritis were treated and the results were good in only two. In two patients with hydrarthrosis the results of treatment were good. A study of the patients over a 14-month period showed that prednisolone trimethylacetate was an effective agent for the intra-articular treatment of inflammation of the knee joint and compared favorably with hydrocortisone used for this purpose.

Before each injection a small amount, usually 3 to 5 ml., of joint fluid was removed for analysis. Viscosity and protein and mucin content were determined, and total and differential leukocyte counts were made. Electrophoresis of the fluid was carried out. The percentage distributions of the various protein fractions were calculated, and from the total protein figure their absolute values were obtained. Marked changes occurred in the cell count of the synovial fluid of patients with rheumatoid arthritis treated with prednisolone trimethylacetate. The initial average cell count was 7,000 per cubic millimeter. The initial proportion of polymorphonuclear cells (75%) dropped by 85% after treatment. The protein level fell from an average of 4.4 to 3.4 Gm. per 100 ml. Most of the patients showed a rise in albumin content and a fall in the alpha, beta, and gamma globulin fractions. There was a progressive reduction in the volume of the joint fluid and an increase in viscosity.

The group of osteoarthritic patients was too small for detailed analysis. The cell changes were similar to those occurring in patients with rheumatoid arthritis. The protein content of joint fluid was lower (3.3 Gm.) and it fell to 2.3 Gm. per 100 ml. after treatment. The albumin content was higher than in the rheumatoid arthritic patients. In the two patients with hydrarthrosis the cell count fell from 14,000 and 40,000, respectively, to 400 and 800 per cubic millimeter. The total protein level dropped from 4.35 to 3.3 Gm. per 100 ml. In other respects the findings resembled those in the patients with rheumatoid arthritis. In all patients the clinical improvement was directly associated with the cell and protein changes described.

Cor Triatriatum.—In cor triatriatum, only 20 cases of which have been described, the left atrium is divided by a septum into two chambers, a posterosuperior which receives the pulmonary veins and an anteroinferior which opens into the mitral valve and left ventricle. Since the septum causes an obstruction at left atrial level, the symptoms, radiologic appearances, and hemodynamics of mitral stenosis may be simulated. The condition is eminently suitable for surgical treatment, yet only three successful cases had been reported until Belcher and Somerville added a fourth (*Brit. M. J.* 1:1281, 1959).

A woman, aged 28, was suspected of having mitral stenosis. She was dyspneic, tired, and suffering from palpitations. The main auscultatory findings were a mitral pansystolic murmur (grade 2) and a loud first sound in the mitral (grade 3) and tricuspid (grade 3) areas. The ECG showed atrial fibrillation and right ventricular hypertrophy. The heart, especially the left atrium, was enlarged and the pulmonary artery was prominent. Cardiac catheterization was unsuccessful. The patient was operated on with a view to correcting the supposed stenosis, when the intra-atrial septum was found. It contained a calcified orifice on the posterolateral aspect. The septum was divided from side to side of the atrium. Immediately the pressures in the pulmonary artery and left atrium fell. Four months later the patient had no symptoms. The venous pressure was now normal, but atrial fibrillation and the mitral systolic murmur persisted. In the four patients with this rare condition who were operated on the diagnosis was only made after exploratory cardiotomy.

The Death of General Practice.—In an article entitled "The Decapitation of General Practice" (*Lancet*, May 16, 1959, p. 1039), Dr. E. Geiringer analyzed what he considered one of the major flaws of the National Health Service (NHS), namely, the payment of general practitioners by capitation fee. Under this system a practitioner undertakes to provide medical care for a fixed annual fee for each patient on his list. If this fee were large and all doctors equally competent and conscientious such a system would provide an ideal medical service, but when this fee is economic for the state and uneconomic for the doctors, who are a heterogeneous group with variable skills and no overwhelming desire to sacrifice themselves, payment by capitation fee encourages them to do less and less for more and more patients. Three results of the nationalization of medicine, the author said, are bad practice, the utility-type practitioner, and the hospitalization of medical practice.

The bad practice falls below all reasonable professional standards. It is conducted from antiquated and badly maintained offices, examinations are perfunctory, equipment is outmoded, no proper records are kept, and treatment consists of the indiscriminate renewal of prescriptions for a dozen or so standard drugs and mixtures. Such practices are still common in industrial areas. Under the per capita system of payment this type of pauper medicine is profitable. A fee-for-service system would eliminate such practices in a few years.

The utility practitioner, on the other hand, is competent, honest, and hard-working. Having accepted the realities of the NHS he tries to make the best of it by having as many patients as possible on his list and giving each a just proportion of his time. The time spent per patient equals the number of hours available divided by the number of patients requiring treatment. By making the latter maximal the time spent on each is minimal. Simple medical care is conscientiously prescribed, but this is the limit of treatment. A patient needing further investigation is referred to a hospital. The numerous psychoneurotic patients are a great worry to the utility practitioner, because he has no time to listen to them. He is not happy to have on his list people who are ill, although he accepts them from a sense of duty. His favorite patients are those who never have any need of his services. Pregnant women go to the nearest antenatal clinic and babies to the infant welfare clinic. Minor surgery is referred to the casualty department of the nearest hospital. Slowly but surely he loses his skill, knowledge, and interest in medicine.

As hospitals expand to do the work of the general practitioner, with special departments and staff for this purpose, a vested interest is created. The public now expects all treatment beyond the most simple to be given in hospital. Every year there are 11,500,000 attendances at hospital casualty departments for minor injuries that could be treated by general practitioners but are treated by relatively inexperienced interns. Litigation favors this. If anything goes wrong the general practitioner is blamed in the courts for not sending the patient to hospital. These considerations apply to a number of other activities that general practitioners have tended to hand over to hospitals and clinics. They include antenatal and postnatal care, deliveries, the care of mother and child, child health, acute infections that could be treated at home, the care of the moribund, and minor psychotherapy. This progressive hospitalization of medical care threatens to abolish general practice in all but name. It is encouraged by medical research, which draws the patient from the home into the hospital for investigation. Hypertension, diabetes, pneumonia, coronary disease, and rheumatism, to mention only a few, have become vested hospital interests. If general practitioners are paid for what they do and not for what they do not do there will be a tendency for them to use modern medical techniques and keep up to date, because then the best practitioners will attract the most patients. There is no reason why general practitioners should not do their own diagnostic radiography and electrocardiography; supervise anticoagulant and steroid therapy; stabilize hypertensive, diabetic, and epileptic patients; and treat patients with pneumonia, acute infections, and coronary disease in the home or in the local hospital. They could cooperate with hospital specialists in treating such patients.

Under the capitation system the introduction of new methods, techniques and investigations into general practice results in pecuniary loss to the doctor because it has to be financed by him. Every day general practice loses something to the hospitals and in return gains nothing. Great Britain now has the most restricted and out-of-date form of general practice of any English-speaking country. The general practitioner has become merely a signer of certificates and a hospital signpost, the author claimed. The existence of a good general practitioner service is essential to inspire the patient's confidence, to insure his continuity of treatment when hospitalized, and to maintain a good consultant service. Healthy and independent general practice exerts a constant pressure on the hospitals and consultants, keeping them efficient and humane. By taking a personal interest in their patients, following their course in hospital, conferring on the spot with hospital colleagues, and having freedom to choose a consultant, general practitioners can prevent complacency, inefficiency, and inhumane treatment in the hospitals. Under the present system consultants can also stagnate professionally because there is no outside pressure from general practitioners to keep them on their toes and be their rivals.

The author made a plea for the resurgence of private medical practice, which would exert a healthy influence on the hospital service and safeguard professional freedom. A salaried service is not the answer; although it would abolish "head-hunting," it would not allow patients freedom to choose their doctors. A bad doctor would still be paid as much as a good doctor. A fee-for-service system would rehabilitate the present moribund service by the working of economic laws. As it is more economic to treat patients in general practice than in hospitals, funds could be diverted from them to an enlarged, better paid, and more efficient general practitioner service. Overtreatment is one of the objections to a fee-for-service system, but this could be checked by making the patient pay a part of each fee charged. Other measures to encourage general practice would be increased facilities and financial incentive for home treatment and general practitioner appointments in local hospitals, which should include inpatient care and supervision.

Cataract Extraction with Alpha Chymotrypsin.—Alpha chymotrypsin (ACT) is an enzyme with fibrinolytic and proteolytic properties, obtained from bovine pancreas. It has a selective solvent action on the zonule supporting the crystalline lens, and when introduced into the anterior chamber of the eye after corneal section it causes complete lysis of the zonule in about three minutes at body temperature. The extraction of 180 cataracts with the aid of ACT was described by Cogan and coworkers (*Brit. J. Ophth.* 43:193, 1959), Ainslee (*ibid.*, p. 200), and Zorab (*ibid.*, p. 202). The ACT was used at a concentration of 1:5,000. Since the solution is relatively unstable at room temperature it was either freshly prepared or stored in a refrigerator until required. Local anesthesia was used for most patients, after premedication with chlorpromazine and pentobarbital. A Von Graefe section was made, followed by peripheral iridectomy, and after irrigating the anterior chamber with Ringer's solution to remove clotted blood the ACT solution was injected through the iridectomy opening. After three minutes the anterior chamber was irrigated to remove the ACT and the lens removed by traction with forceps or by suction. It was removed easily, since there was no suspensory ligament holding it back. The removal of senile and presenile cataracts is made much easier by the use of ACT, which does not damage any of the ocular structures. No serious complications occurred during the operations.

Atomic Fall-out Hazards.—Mr. Macmillan, the Prime Minister, in a statement before Parliament, said that even if the deposition of radioactive strontium (Sr^{90}) that has already been released into the stratosphere from nuclear explosions continues at the higher rate recently observed, its concentration in bone is unlikely to approach the level which would require immediate action. For several years measurements of the deposition of Sr^{90} and other radioactive isotopes have been made. Recent measurements indicate that the rate of deposition in rainfall is double that of a few years ago. Analysis of fall-out material shows that Sr^{90} can remain in the stratosphere for many years before being deposited on the earth. The annual fall-out is about 12% of the stratospheric content. Once radioactive materials have left the stratosphere and entered the troposphere the local rate of deposition depends largely on rainfall. Heavy rainfall increases fall-out, and this was one of the factors responsible for the high fall-out in 1958. The atomic bomb tests conducted in the U. S. S. R. last year were also contributory. The Argus experiments made at the same time in the United States resulted in only a small addition to the radioactivity of the stratosphere.

In Britain regular measurements are made of Sr^{90} in food, milk, drinking water, air, soil, and vegetation. Samples are regularly collected from 200 depots handling 40% of the milk consumed in the country. Cereals and vegetables, both home grown and imported, are also tested. The results of the 1958 food survey are now being prepared for publication. They indicate that the amount of Sr^{90} in food and drinking water gives no cause for alarm. Most of that present in milk is due to the isotope that has been freshly deposited on grass before it has a chance to be washed into the soil. If the enhanced fall-out of 1958 were to continue in 1959 an increase in the Sr^{90} of the diet could be expected, but Mr. Macmillan assured Parliament that its concentration in human bone was not a cause for anxiety. The Sr^{90} concentration found in 1958 in the bones of stillborn children and in those dying from various causes was only slightly above that of the previous year. The irradiation of human bone and marrow from Sr^{90} is less than that due to the natural background irradiation to which all are exposed.

Mr. Macmillan stated that cesium-137 is not readily taken up from the soil by plants and is not retained in the body for long periods. The chief danger is a genetic one, although gonadal exposure is small in relation to natural background irradiation. The absorption of plutonium from fall-out is low in comparison with that of Sr^{90}. Carbon-14 has been measured in air and foods for many years. Most of it comes from cosmic radiation, but a small amount also comes from atomic explosions. Its concentration is being kept under review because of its long persistence.

Qualified but Unable to Practice Medicine.—Nationals of British colonies who wish to practice medicine in their own countries after qualifying abroad often find it difficult to do so. The law prevents their practicing unless they have a qualification which is recognized in the colony, which usually means one that is registerable in Great Britain. In the last year 300 students from British colonies were working in medical schools in Canada and the United States, and about 450 were pursuing premedical studies, but as Great Britain has no reciprocal arrangement with the United States, nor with 4 of the 10 Canadian provinces, medical qualifications obtained in any of the approved American or in 8 of the 12 Canadian schools are not recognized in British colonies. Hence, most of these students will be legally prevented from practicing in their homeland, however good the status of their medical school or excellent their record. They must first seek additional qualifications from Great Britain or from a country that has established reciprocity with Great Britain.

Doctors from most islands in the West Indies, Trinidad, the Leeward Islands, Hong Kong, North Borneo, Kenya, Rhodesia, Uganda, and Fiji are required to hold a qualification registerable in Great Britain. Those from the Bahamas, Bermuda, British Honduras, Cyprus, Singapore, and Tanganyika who qualify outside Britain may be permitted to practice in some precarious form of temporary and localized licensure, or by legal subterfuge. Others are more fortunate. Thus, physicians from the Tonga Islands can be registered if trained in American schools. In Jamaica physicians may take the examinations without retraining, but in the Barbados registration is curiously confined to those entitled to practice in New York state, and in British Guiana it is open to those with a degree from a medical school approved by the American Medical Association. Nigeria has recently opened its doors to those persons holding the diploma of the National Board of Medical Examiners in the United States. In spite of the high academic standing of the medical schools of McGill or Toronto universities in Canada, qualifications obtained there are not acceptable, because these schools do not maintain reciprocity with the General Medical Council of Great Britain.

The avenue of the American-trained student is usually through one of the Canadian schools having reciprocity with Great Britain, but this requires time and money after the qualifying examination. As a result of these restrictions many British colonials are settling in the countries in which they were trained, while their own countries remain desperately short of doctors. There is still only one physician to every 50,000 persons in Nigeria. It has been suggested that wherever the colonial medical student may have studied he should be able to take a local registration examination preceded by a local internship. This could be controlled by a Commonwealth Board of Medical Examiners, which would be charged primarily with exploring the prospects of extended intern posts for approval and assisting in the local examinations.

Tranquilizer Hazards.—A report on hypnotic, sedative, tranquilizing, or stimulating drugs that can be bought at drug stores without prescription was sent to the Minister of Health by the recently formed Advertising Inquiry Committee. The medical panel of the committee drew up the report after a survey of advertisements in the press and on television. There is a British Code of Standards on the advertising of medicines and surgical appliances to the public and in the opinion of the panel this is not being observed. The report stated that 25 well-known brands of drugs that are potentially lethal, particularly in the hands of children or potential suicides, can be bought without a prescription. A person with suicidal intent can go into six drugstores in succession and purchase a lethal quantity of some of these drugs. Another hazard is the morbid dependence of some persons on such drugs. The committee believes that there is a strong case for making all of these drugs prescription items. The report also suggests that there should be a controlled survey to ascertain the extent of self-medication and that an independent body should be set up to test the claims of advertisers. Statements made about a drug or remedy often contain a reference to a "new" or "recently developed" substance with special properties. The precise nature or composition of the substance is seldom or never given, and the advertising material in such cases makes its appeal to the current worship of science.

Coronary Angiography.—Coronary angiography is being developed in the department of cardiology, St. George's Hospital, London. This is the only method of obtaining information on the condition of the coronary arteries during life. The ECG only reveals the condition of the heart muscle. It is desirable to detect narrowing and calcification of the coronary vessels in the early stages of the disease and to assess the value of operative procedures, diet, and anticoagulants in the treatment of coronary disease. Coronary angiography should also help in the selection of patients for operation. The procedure is carried out by advancing a catheter along the brachial artery until it is within an inch of the aortic valves. This is done under radiographic control with use of an image intensifier. The injection of radiopaque medium into the catheter is made against the aortic valves as the ventricles contract. It enters the coronary vessels and its course is followed by cineradiography.

CORRESPONDENCE

ALCOHOL AND MOTOR ACCIDENTS

To the Editor:—It has become increasingly obvious that the influence of alcohol is the most frequent human factor responsible for serious motorcar crashes. The records of Dr. S. R. Gerber at the county coroner's office, Cleveland, for the last 19 years show that 46% of the pedestrians, 54% of the drivers, and 42% of the passengers had been drinking. Since these figures include deaths up to 12 hours after the crash, Dr. Gerber points out that some of the victims tested had survived a sufficient length of time to metabolize alcohol present at the time of the "accident," and, therefore, contributed to the number of negative tests.

A recent study by Haddon and Bradess from Westchester County, New York, revealed that 87 drivers had died within four hours of their single-vehicle crash. Eighty-three, or 95%, of these had had blood alcohol level determinations. Of the 83, 73% had been drinking; 69% had blood alcohol levels over 0.05%, and 49% had levels of 0.15% or more. Figures from other widely scattered areas over the United States show similar percentages, and if this can be assumed to hold for the nation as a whole, about 50% of the 30,000 nonpedestrian deaths each year can be attributed to the drinking driver.

It has become accepted by the courts throughout the land that a driver whose blood alcohol level reads 0.15% or less is not "under the influence" of alcohol. This 0.15% reading means that, for a 150-lb. (68-kg.) person, 6 oz. of 100-proof liquor have been distributed throughout the blood, tissues, and brain. To attain this blood alcohol level, about 7 or 8 oz. need to be swallowed in about an hour; and this is 100-proof material, not the usual 86-proof or 90-proof.

Two events of significant impact on this problem have occurred in the last few months.

At the Indiana University Symposium on Alcohol and Road Traffic, Dec. 12-14, 1958, the following statement was prepared: "It is the opinion of this Committee that a blood alcohol concentration of 0.05% will definitely impair the driving ability of some individuals and, as the blood alcohol concentration increases, a progressively higher proportion of such individuals are so affected, until at a blood alcohol concentration of 0.10%, all individuals are definitely impaired." This was signed by a significant group of the outstanding authorities in the alcohol-motorcar field. At long last, the unrealistic figure of 0.15% may perhaps be displaced by a blood alcohol level more practically related to the role of the drinking driver in our traffic deaths and injuries.

A second important event is the publication by the American Medical Association of a Medical Guide for Physicians in Determining Fitness to Drive a Motor Vehicle (*J. A. M. A.* 169:1195-1207 [March 14] 1959). It is significant that the news services, in commenting on this new manual, devoted most of their space to the alcohol section.

With this recognition, the next need is implementation. The first step here is the passage of legislation by all states making it virtually certain that a driver suspected of driving after drinking be subjected to chemical tests to prove whether alcohol, or some other factor, is the cause of his unusual behavior. Five states, led by New York, and followed by Kansas, Idaho, Utah, and North Dakota, have taken this necessary step. Legislatures of some 20 other states have considered and, so far, have refused or neglected to enact this life-saving measure.

Nothing will so surely reduce the number of drinking drivers on our highways as prompt conviction for drinking charges, and nothing will so surely lead to conviction as incontrovertible, objective evidence of drinking while driving; but we need more than this. We need courts and prosecutors who will use the evidence at hand. At the moment, the weak link in the drinking-driving problem is the prosecution. The records of every state are replete with long case histories of drinking drivers who have had repeated arrests, only to be released, until they have killed themselves and one or more others in their final drinking-driving violation.

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"NUCLEAR SEX"

To the Editor:—While determinations of "nuclear sex" by the techniques described in the editorial in The Journal, June 6, 1959, page 678, gave the first clues to the remarkable nature of cellular sex in Turner's and Klinefelter's syndromes, even more fundamental observations have been made recently and should be brought to the attention of those who read that editorial. These syndromes and mongolism are the first human diseases to be associated with the loss or addition of a chromosome. While previously unidentified in man, the effects of such abnormal karyotypes are well known in nonmammalian species.

The indirect methods of determining so-called nuclear sex have been able to distinguish between normal males and normal females, but the dichotomy fails in situations like Turner's and Klinefelter's syndromes. The sex chromosomes of such patients are neither those of the normal female (X X) nor those of the normal male (X Y) in all cases so far reported. The cells from patients exhibiting Klinefelter's syndrome have contained a Y and two X chromosomes (which raises the total number from 46 to 47). Cells containing but one sex chromosome, and that an X, giving a total of 45 rather than 46, have been found in Turner's syndrome.

Inferences, based on the presence of Barr chromatin (Barr and Bertram, *Nature* 163:676, 1949), such as, "the genetic sex has proved to be female in many of the clinically recognized cases [of Klinefelter's syndrome]," are now known to be incorrect. If Barr chromatin were reported to be "present" or "absent," rather than "male" or "female," such errors might be reduced. What is needed is exact information as to the numbers and kinds of chromosomes present. Those interested in disorders of human chromosomes or the diseases they produce should consult the papers and editorial which appeared in the *Lancet*, April 4, 1959; the correspondence in the April 18 and April 25 issues; and the references therein. The contributions of cytogenetics to our knowledge of man are just beginning.

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SPONTANEOUS REGRESSION OF MALIGNANT DISEASE

To the Editor:—Your guest editorial on spontaneous regression of malignant disease, in The Journal, April 11, page 1758, stated that the theory for spontaneous regression of malignant tumors had not been advanced. The theory for disappearance can be evolved from the research work of biochemists Dulkin and Lobstein of the Research Foundation for Diseases of the Eye. They found that lysozyme, an enzyme found in body fluids and in tears, in addition to being bacteriostatic, is carcinostatic for certain tumors in rats. The work, which resembles Fleming's experiments with penicillin in the manner of procedure, is promising. Clinical trials have not been made.

Other body enzymes may also be carcinostatic. Experiments are planned to determine whether lens epithelium secretes carcinostatic substances. Cancer has not been reported in the lens. The progress of cancer is like that of other diseases—a struggle between host resistance and the virulence and degree of malignancy. The chief factor in host resistance may be lysozyme and other body enzymes.

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MEDICAL FILM REVIEWS

HOSPITAL SEPSIS: A COMMUNICABLE DISEASE

The premiere showing of "Hospital Sepsis: A Communicable Disease" drew a capacity audience at the Annual Meeting of the American Medical Association, Atlantic City, June 8. This film, which was produced in cooperation with the American College of Surgeons, American Hospital Association, American Medical Association, and Johnson and Johnson, is now available from the A. M. A. Motion Picture Library for showing to physicians and hospital groups.

Portion of capacity audience at premiere showing of "Hospital Sepsis: A Communicable Disease."

Culdoscopic Technique and Cinematography: 16 mm., color, sound, showing time 19 minutes. Prepared by Albert Decker, M.D., and Irving H. Saxe, M.D., New York. Produced in 1958 by Audio Productions, New York, for and procurable on loan from Schering Corporation, Bloomfield, N. J.

The instruments, the position, and the step-by-step technique used in culdoscopic examination of a patient are demonstrated in this film. Representative pathology and normal pelvic anatomy as seen through the culdoscope are shown by means of an 8 mm. reflex camera. The pathology includes fimbrial adhesions, unruptured tubal pregnancy, tubal abortion, tubal peristalsis, appendicitis, and salpingitis. Not too much time is spent on technique, but it is adequate. Two patients are shown, followed by a number of examples of various types of ovarian, tubal, and uterine pathology. However, the whole procedure looks so smooth and readily done that the viewer is likely to get a wrong impression about the ease of the operation. This is an excellent film. The principles enunciated are sound, and the film is recommended to anyone interested in the procedure of culdoscopy.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Heart Failure in Patients with High Blood Pressure. J. N. Mickerson. Brit. Heart J. 21:218-224 (April) 1959 [London].

In an attempt to assess the causes of heart failure, a common complication and a major cause of death in patients with high blood pressure, the author studied 184 men and 157 women with hypertension, who were admitted in heart failure to the Charing Cross Hospital in London. A cause of heart failure in addition to hypertension was found in all but 10 (3%) of the 341 patients. Ischemic heart disease precipitated heart failure in 172 (50%) of the 341 patients, and in an additional 48 patients (14%) it probably contributed to the heart failure. Other important causes of heart failure were valvular lesions in 37 patients (11%), renal disease, alone or combined with cardiac lesion, in 50 patients (15%), respiratory infection in 20 patients (6%), and malignant hypertension in 29 patients (9%). The remaining less frequent causes of heart failure in 23 patients (6.6%) were combined to form a miscellaneous group. The presence of a renal lesion doubled the mortality rate and reduced by 12 years the average age at death when compared with patients without renal damage, whose average age at death was 66.1 years and among whom the mortality rate was 21%. Patients with evidence of renal disease had the highest blood pressures. The worsening prognosis of patients with hypertension and heart failure with rising blood pressure levels was shown to be due to the presence of a renal lesion rather than to the height of the blood pressure per se.

The Pulseless Syndrome. M. H. Lessof and L. E. Glynn. Lancet 1:799-801 (April 18) 1959 [London].

The authors are of the opinion that clinical case reports that have been published under the heading of "pulseless disease" describe a syndrome rather than a disease entity. Obstruction of the large arteries arising from the arch of the aorta may be due to several causes, including syphilitic aortitis, healed dissecting aneurysm, trauma, atheroma, and congenital vascular anomalies. Even when these conditions are excluded, the reported cases of arteritis of medium-sized and larger vessels do not always correspond with those in young Japanese women described by Takayashu in 1908. By common usage, pulseless disease implies an absence of pulses in the arms and sometimes in the neck, together with evidence of an inflammatory reaction, such as fever, increased erythrocyte sedimentation rate, and raised serum globulin level, or else histological evidence of arteritis near the origin of large vessels. These features were present in the 3 women reported, who ranged in age from 21 to 39 years. All 3 women presented with loss of pulses in both arms, but the underlying diseases were different. One had obliterating brachiocephalic arteritis of Takayashu; the second had an unidentified thrombotic condition of the large arteries; and the third had arterial occlusion associated with systemic lupus erythematosus. Blood flow studies in the limbs helped to define the extent of peripheral arterial involvement, even when symptoms were absent.

Some Patients with Unusually High Digitalis Requirement. P. Kirketerp. Ugesk. laeger 121:496-498 (March 26) 1959 (In Danish) [Copenhagen].

Kirketerp cautions against adherence to a standardized digitalis dosage. In the 5 patients reported, who had been seen over an 8-year period in a medical department of moderate size, the digitalis need was found to be 2 or 3 times that of the ordinarily used dose of 100 mg. of folium digitalis 6 times weekly. For these patients the larger digitalis dose meant a decisive change for the better in their clinical condition. The author advises the physician to bear in mind that now and then there will be a patient who is not helped by digitalis until he receives a dose essentially higher than that usually prescribed.

Differential Pulmonary Artery Occlusion in Patients with Chronic Pulmonary Disease. B. L. Charms, B. L. Brofman and A. Adicoff. Am. J. Med. 26:527-533 (April) 1959 [New York].

Five patients with pulmonary disease, either localized or generalized, were subjected to hemodynamic studies. The technique of balloon occlusion of first one and then the other of the main branches of the pulmonary artery was used. With

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The place of publication of the periodicals appears in brackets preceding each abstract.

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localized pulmonary lesions, occlusion of the pulmonary artery supplying that area diminished or abolished venous admixture due to a diminished local ventilation-perfusion relationship. Increase in flow through pulmonary lesions by occlusion of the opposite pulmonary artery caused an increase in venous admixture and further fall in systemic arterial oxygen partial pressure and hemoglobin saturation. Cardiac output, pulmonary artery pressure, and respiratory minute volume changes closely paralleled changes in arterial oxygen content. The method of temporary unilateral pulmonary artery occlusion proved to be a useful adjunct in evaluation of patients with pulmonary lesions, especially in determining pulmonary resectability when diffuse disease was also present. Pulmonary arteriolar and total pulmonary resistances were calculated with use of pressure distal to an occluding balloon; this is not necessarily the same as a control wedge pressure. Only small increases in resistance were observed with respect to the increase in flow produced in the unoccluded lung, and calculated resistance actually fell to approximately one-half of assumed control level.

Pulmonary Artery Stenosis. H. A. Shafter and H. A. Bliss. Am. J. Med. 26:517-526 (April) 1959 [New York].

The authors add 5 patients with stenosis of the pulmonary artery to the 28 previously described. The 5 patients were observed in the course of 18 months. Two had no other apparent lesions of the heart or great vessels; 3 had evidence, by catheterization of the right side of the heart, of ventricular septal defect, probable common atrioventricular canal, and patent ductus arteriosus respectively. None had pulmonic valve stenosis. A study of the 5 patients and a review of the literature reveal some helpful clues to the diagnosis, and raise important questions about the etiology, physiological significance, and treatment of this lesion. The clinical diagnosis of pulmonary artery stenosis is frequently hampered by coexistent cardiovascular lesions. A continuous murmur should make one think of the diagnosis. The lesion commonly produces a systolic murmur, which may be heard with maximal intensity at the base of the heart several centimeters lateral to the sternal border. Pulmonary artery pressure rises abruptly when the cardiac catheter is withdrawn through the narrowed segment. In the absence of pulmonary artery narrowing, patent ductus arteriosus probably does not produce such a pressure change. The appearance of a constantly narrowed pulmonary artery segment on angiocardiographic study strengthens the diagnosis.

Although pulmonary artery stenosis may in most patients originate as a developmental anomaly in fetal life, the possibility that it occasionally occurs as an acquired lesion at some time after birth must be examined. Some evidence suggests that either pulmonary artery thrombosis or "natural transformation" of the pulmonary artery resulting from prolonged rapid pulmonary blood flow may occasionally produce pulmonary artery stenosis. The term "natural transformation" was used by Gasul and associates in describing the narrowing of the right ventricular outflow tract which, developing gradually over a number of years, may reduce the left-to-right shunt in patients with ventricular septal defect. One may inquire whether or not the prolonged increase in pulmonary blood flow in other patients with left-to-right shunt may in time produce "natural transformation" of the pulmonary artery, i. e., pulmonary artery stenosis, with consequent lessening of the shunt.

The physiological significance of stenosis of the pulmonary artery depends upon the resistance it offers to right ventricular outflow. Resistance mainly depends upon the physical characteristics of the narrowing, i. e., upon its length and lumen. A lesion causing only a small pressure gradient at rest may with exercise produce significant right ventricular hypertension. In most patients, pulmonary artery stenosis does not cause serious hemodynamic abnormalities. If these are present, however, surgical repair may be possible and desirable.

Neuroendocrinic Syndromes in the Course of Tuberculous Meningitis. L. Pertoni and R. Bistaffa. Riforma med. 73:327-331 (March 21) 1959 (In Italian) [Naples].

Neuroendocrinic syndromes were observed in 4 of 49 patients with tuberculous meningitis seen by the authors between 1948 and 1957. The first patient, a 29-year-old woman, some weeks after clinical recovery from the meningitis and dismissal from the hospital, complained of an abnormal and marked libido which lasted for a few months. The second patient, a 13-year-old boy, while recovering from the meningitis after months of treatment, suffered polydipsia and polyuria; a diagnosis of diabetes insipidus was made, and the patient recovered from the latter disease after a period of about 2 years. The third patient, a 21-year-old man, died 8 months after admission to the hospital; on autopsy, signs of pulmonary tuberculosis, meningeal irritation, and a caseous focus in the right adrenal gland were observed. The fourth patient, a 17-year-old youth, 6 months after treatment, while showing signs of recovery from the meningitis, suffered bulimia which disappeared after a few months. The authors believe that in the first and fourth patients the neuroendocrinic syndromes were the result of streptomycin given for the treatment of tuberculous meningitis; streptomycin, acting as a stimulant, caused a hyperfunction of the diencephalon and of the adrenal gland; the syndromes regressed with the suspension of treatment. In the second patient the neuroendocrinic syndrome was more likely connected with the process of a basal arachnoiditis.

Some Pathogenetic and Clinical Aspects of Pulmonary Tuberculosis with Respect to Intercurrent Influenza Episodes. N. Montanini, G. Pallotta and G. De Ritis. Ann. Ist. Carlo Forlanini 18:370-384 (no. 4) 1958 (In Italian) [Rome].

The relationship between pulmonary tuberculosis and influenza was studied in a group of 43 patients with tubercular pulmonary lesions, at different clinical and roentgenologic stages, who contracted Asian influenza in 1957. In most patients the influenza reactivated the apparently inactive tubercular lesions; relapses occurred in some patients who had been dismissed from the hospital for a long time either because they had clinically recovered or because their condition was stationary. None of these patients at the moment of contracting influenza was taking tuberculostatic drugs. Influenza had no effect on the condition of hospitalized patients with active pulmonary tuberculosis who were being treated with antibiotics; they were deriving benefit from the treatment and showed no resistance to the drugs. Influenza, however, caused death in most chronic tuberculous patients who showed resistance to all antibiotics. The authors believe that treatment with isoniazid should be continued periodically, and for a long time, until there is complete recovery in patients who have recovered only clinically or whose condition is stationary. Treatment with isoniazid is necessary in case these patients should contract virus infections.

The Volume of N/10 Hydrochloric Acid Neutralized Per Day in the Treatment of Peptic Ulcer. E. A. Marshall and D. Samon. Am. J. Gastroenterol. 31:389-397 (April) 1959 [New York].

The authors observed 3,877 patients with roentgenologically confirmed peptic ulcer. Nine hundred ninety-two of these patients had had hemorrhages one or more times before being seen; 430 had nonstenotic obstruction; and in 159 the ulcer had previously perforated. Complications had been encountered in 1,582 patients, and the remaining 714 had symptoms of uncomplicated ulcer. Treatment was based especially on the consideration that at least 14 liters of N/10 hydrochloric acid must be neutralized each day in order to inactivate the corrosive effects of acid in peptic ulcer and permit the patient to ingest an unrestricted diet without symptoms. For neutralization the authors depended on aluminum hydroxide and calcium carbonate. The medicaments were administered at half-hour intervals for 16 hours a day, at bedtime, and 2 and 4 hours after retiring. This schedule was not changed for 4½ months. The use of the roentgenogram as a criterion of the healed ulcer was regarded as inadequate. A patient who upon completion of the intensive medical treatment was able to ingest a completely unrestricted diet for more than a year without symptoms, and without any subsequent antacid medication, was considered to have a healed ulcer. A patient who 24 hours after initiation of a program of sufficient sedative, alkalizing, and adsorptive drugs was able to ingest a completely unrestricted diet without distress was presumed to have a "healing" ulcer. Treatment resulted in healing in 83.4% of the 3,877 patients. The remaining 16.6% required that 19.5 liters of N/10 hydrochloric acid or 71 Gm. of pure hydrogen chloride be neutralized each day; two-thirds of these (7.6% of the total group) were therapeutic failures. Follow-up studies on 1,278 patients showed that most of them remained healed for 3 or more years.

Epidemiologic and Clinical Observations in Sarcoidosis. M. M. Cummings, E. Dunner and J. H. Williams Jr. Ann. Int. Med. 50:879-890 (April) 1959 [Lancaster, Pa.].

Sarcoidosis was diagnosed in 1,700 patients seen in Veterans Administration hospitals between 1949 and 1956. The case records of 1,194 of these patients whose conditions were diagnosed during the 5-year period 1949-1954 were reviewed. Information concerning age, race, sex, place and date of birth, and place of initial hospitalization was analyzed. The most striking observation was the geographic distribution of the disease, revealing an endemic area in New England and the North Central States. The rural location of birthplace and the predominance among Negroes, observed by Michael, were confirmed in this study. The distribution of birthplaces of veteran patients given a diagnosis of sarcoidosis correlated better with a pine forest environment than it did with the sandy soil suggested by Gentry. Lumbering and wood milling were designated as the leading industries in the high sarcoidosis prevalence areas.

A detailed clinical analysis of 256 records selected at random from those of the 1,700 patients was then undertaken. This was done to evaluate the diagnostic criteria utilized in widely scattered hospitals, and to learn more about the natural history of the disease. The criteria used for diagnosis in the study of the 256 records are those defined by a subcommittee of the National Research Council in 1956. According to these, sarcoidosis is a systemic disease, or group of diseases, of undetermined etiology and pathogenesis. Histologically, it is marked by the presence of epithelioid-cell tubercles, showing little or no necrosis. Varying types of inclusions in giant cells may be present but are not pathognomonic. A similar histological picture may be found in certain other diseases, especially in infectious granulomas and in beryllium poisoning. Clinically, the disease most commonly involves lymph nodes, lungs, skin, eyes, liver, spleen, and phalangeal bones. The course is usually chronic, and constitutional symptoms vary. While the intracutaneous tuberculin test is frequently negative, a positive test does not controvert the diagnosis.

When an effort was made to apply these criteria more critically than the reporting hospitals had done, 81 cases were eliminated, and 175 cases, in which biopsy had confirmed the diagnosis, were studied further. As classified by race, 76 patients were white, and 99 nonwhite. Since 10% of American veterans are Negroes, the frequency of sarcoidosis among Negroes was 12 times greater than among whites. It was learned that sarcoidosis with biopsy confirmation may still at times be confused with other diseases, particularly those which may lead to granulomatous reactions. Sarcoid reactions to neoplastic diseases, as well as to tuberculous or fungous infections and beryllium disease, must be kept in mind. Sarcoidosis does not appear to be so benign as is generally reported. A follow-up study revealed that 15% of the veterans with sarcoidosis died within a 5-year period. The most frequent cause of death was cor pulmonale. Active tuberculosis was a not infrequent finding. Certain laboratory findings suggested that pine pollen may be added to the list of agents thought to be responsible for the disease or syndrome, sarcoidosis.

The Clinical Value of Renal Biopsy. D. J. Deller, V. J. McGovern and R. Reader. M. J. Australia 1:481-486 (April 11) 1959 [Sydney].

The authors report on 53 aspiration renal biopsies performed successfully on 51 patients after 59 attempts. Renal tissue was obtained from the cortex and medulla in 52 cases and from the medulla only in 1. The average number of glomeruli contained in a biopsy specimen was 16. Certain difficulties in technique are discussed, but, in general, they were not great. Complications after renal biopsy were uncommon. In one patient necrotizing papillitis occurred and required nephrectomy. In 2 patients a preexisting infection appeared to be aggravated. The relationship between biopsy and these complications is not clear. The clinical diagnosis was confirmed by biopsy in 22 of the 51 patients; the clinical diagnosis was compatible with the histological findings in 10; the clinical diagnosis was changed as a result of biopsy in 13; and in the remaining 6 neither the clinical nor the biopsy features were sufficiently characteristic to be of definite significance. The diseases which biopsy showed to be present most frequently, when not thought likely clinically, were either chronic pyelonephritis or chronic glomerulonephritis.

Renal biopsy may be of value in the management of patients with the nephrotic syndrome, hypertension, and miscellaneous renal diseases. An etiological diagnosis may be provided by biopsy in patients with the nephrotic syndrome, and the severity of the lesion assessed. Information of value concerning prognosis and therapy may be obtained. In patients with hypertension, renal biopsy can usually confirm or exclude chronic glomerulonephritis. Renal biopsy led to an unexpected diagnosis in 5 patients with obscure renal disease, as follows: 1. Focal embolic glomerulonephritis was shown in one patient in whom the diagnosis of subacute bacterial endocarditis had not been seriously considered. 2. The presence of moderately severe diabetic glomerulosclerosis in a young woman with diabetes mellitus, who was clinically well and desired a pregnancy, modified the physician's approach to her case. 3. Chronic glomerulonephritis was revealed in a boy with a symptomless proteinuria, and this finding helped the general physician in the advice he gave to the child's parents. 4. Lupus nephritis was strongly suggested by renal biopsy in a young woman with a clinical diagnosis of pyelonephritis. 5. Renal biopsy disclosed normal tissue in a woman 5 months pregnant who was considered clinically to have chronic glomerulonephritis and who progressed to term without complication.

Renal biopsy has a definite but limited value in clinical practice. It is no substitute for the more usual diagnostic procedures and techniques, and must be considered in the light of these methods. It is not a short cut in the diagnosis of renal diseases, for problems arise in sampling and pathological interpretation.

Treatment of Acute Hemorrhagic Pancreatitis with Cortisone. C. Lacerenza. Minerva chir. 14:305-309 (March 15) 1959 (In Italian) [Turin, Italy].

The cases of 6 patients, ranging in age from 28 to 52 years, with acute hemorrhagic pancreatitis are reported. Four patients were male, and 2 were female. After surgical treatment each patient received antibiotics and 100 to 200 mg. of cortisone per day. A pancreatitic relapse was suspected in the first patient, and the symptoms were checked with antibiotics and cortisone. After this patient suffered a third relapse, treatment with cortisone was not as effective as during the previous 2 courses, but his clinical condition improved markedly and rapidly. One patient, a 28-year-old woman, died of acute yellow atrophy of the liver after choledochostomy and cholecystectomy. Antibiotics in another patient, a 43-year-old woman, caused diarrhea which provoked a sudden diminution of the diuresis; this complication was checked with 15 units of human plasma and erythromycin. Cortisone had a good effect on the symptoms in all the patients and caused a marked drop in the serum amylase. The blood sugar level, which was high in some patients, became normal in a few days. The drug was also effective in relapses.

Corticotropin (ACTH) and the Adrenal Steroids in the Management of Ulcerative Colitis: Observations in 240 Patients. J. B. Kirsner, W. L. Palmer, J. A. Spencer and others. Ann. Int. Med. 50:891-927 (April) 1959 [Lancaster, Pa.].

The authors summarize their experience with corticotropin (ACTH) and the adrenal steroids in ulcerative colitis during the period from January, 1950, to November, 1957. The series comprised 240 patients, each of whom had been under observation for at least one year; none had responded satisfactorily to conventional medical management. The patients included 128 males and 112 females, mostly in the younger age group. The colitis had been of long duration, exceeding 5 years in 168 of the patients. Roentgenologic evidence of colitis was demonstrated in most patients, involving the entire colon in approximately 50% of them. Complications had preceded steroid therapy in 210 of the 240 patients. Blood transfusions had been required in approximately one-half of the series; approximately 100 patients had been advised elsewhere to undergo colectomy and ileostomy. The colitis was classified as mild in 12 patients, moderate in 86, and severe in 142. The objectives of therapy included the reestablishment of normal intestinal function, the restoration of nutrition, and the resumption of a normal life. The over-all response to combined medical and steroid therapy was classified as good in 115 patients, moderately favorable in 80, and minimal in 45.

Corticotropin, given intravenously and intramuscularly, was the most potent compound, followed by intravenously administered hydrocortisone. In oral administration, however, prednisone and prednisolone surpassed hydrocortisone on a milligram basis in a ratio of 2:1, the therapeutic effects being approximately similar with such doses. A favorable response consisted of the rapid disappearance of fever, toxemia, bloody diarrhea, and abdominal discomfort; appetite improved, and there was an increased sense of well-being. Proctoscopic improvement occurred more slowly than did the clinical response. Laboratory indications of improvement were the return of elevated sedimentation rates to normal, disappearance of blood from the stools, improvement in the anemia, restoration of normal patterns of plasma proteins, and, in serial biopsies, histological evidence of healing.

Steroid therapy has been continued in 101 patients; in 63 of these remissions persist, but there have been recurrences, often less severe than previously, in 38. The steroids have been considered to be very helpful in 46, helpful in 48, and ineffective in 7 instances. Eighty-nine patients are leading useful lives, while 12 are variously incapacitated but are not invalids. Steroid therapy has been discontinued in 99 patients, 59 of whom experienced recurrences. Remissions have been sustained in 40 cases, lasting longer than one year in 37. Steroids have been judged as very helpful in 47 persons of this group, helpful in 28, and ineffective in 24; 86 persons are leading effective lives, while 13 are variously incapacitated. The most important problems were emotional difficulties in 40 patients (including 3 suicides), infections in 43, and severe hypercorticism in 35. Perforations of the small intestine and peritonitis occurred in 2 patients. Surgery was necessary in 26 patients (11%). The indications were as follows: minimal or decreasing response to medical treatment, 10 cases; fulminating disease, 5; uncontrollable hemorrhages, 4; possible carcinoma, 2; polyps, 2; resection of apparently localized disease, 2; and intestinal obstruction, 1. Twenty of the 26 patients operated on survived. Twenty-three patients (9%) died, 6 of causes related to the colitis, 7 of complications associated with steroid therapy, and 10 of causes unrelated to ulcerative colitis or the use of steroids. Corticotropin and the adrenal steroids (hydrocortisone, prednisone, and prednisolone), though not curative, are highly effective adjuncts in the treatment of ulcerative colitis. The effects of the steroids surpass the response to any other therapeutic procedure.

Sacro-Iliitis in Reiter's Disease. J. K. Oates and A. C. Young. Brit. M. J. 1:1013-1015 (April 18) 1959 [London].

The authors report on 76 men and 2 women with Reiter's disease, 46 of whom had suffered more than one attack of the disease. All the patients had arthritis involving one or more joints associated with urethritis. Some of the patients also had conjunctivitis or iritis. Involvement of the sacroiliac joints was revealed by roentgenologic examination in 35 patients (44%). Nine patients (11.5%) showed doubtful evidence of roentgenographic abnormality of the sacroiliac joints, and 34 (43.6%) had roentgenographically normal joints. Sixteen (45.6%) of the 35 patients, 3 (33%) of the 9 patients, and 5 (14.7%) of the 34 patients complained of backache. Twelve (34%) of the 35 patients had iritis, compared with only 3 (8.8%) of the 34 patients. The attacks of iritis were recurrent in 9 of the 12 patients and were usually the only manifestation of the disease.

Sacroiliac disease revealed roentgenographically is common in patients with Reiter's disease. Clinically, appreciable involvement of these joints is probably common only during the acute stages of the disease, but the diagnosis may be easily missed. In patients with Reiter's disease special attention should be paid to the presence, site, and distribution of backache. Sacroiliac disease in this condition often appears to be associated with recurring attacks of iritis. This iritis is usually the only symptom. The occurrence of frequent attacks of iritis in men should always lead to inquiry into the presence of a past history of Reiter's disease or its components. Evidence of sacroiliac disease and genital infection should be carefully sought in such patients.

SURGERY

The Dynamic Pharyngeal Flap: Its Selective Use and Electromyographic Evaluation. T. R. Broadbent and C. A. Swinyard. Plast. & Reconstruct. Surg. 23:301-312 (April) 1959 [Baltimore].

Good speech is the goal in the management of any anatomic or physiological abnormality of the palate. The pharyngeal flap has received considerable interest, but its use as a dynamic muscular unit, rather than a static bridge, has not been clarified. The investigations described extended over a 4-year period and were designed to demonstrate the functional or static nature of the pharyngeal flap. The preoperative and postoperative management and the basic operative procedure have been described and illustrated by earlier investigators whom the authors mention in a historical review. Some aspects of the procedure are commented on by the authors, who performed pharyngeal flap operations on 49 patients. Speech deficiency was caused by cleft palate in 35 patients, and in the other 14 the speech defect was due to congenital paresis, to hemiplegia, to postoperative or postinfectious paresis, to poliomyelitis, or to postoperative defect in the palate.

The operation is done under general, transnasal, endotracheal anesthesia. Nasal intubation affords greater working space within the mouth and pharynx than oral intubation and also allows for attachment of the flap to the posterior palatal surface with greater ease. The endotracheal tube can be shifted from side to side, gently, easily, and safely, without the production of laryngeal edema, during elevation of the flap. During attachment of the flap, the tube occupies one posterior nasal aperture without producing abnormal tension on the flap. The selected use of the flap will determine its length, width, and position of its base. Lateral incisions are made on either side of the posterior pharyngeal wall, and the mucosa and the posterior pharyngeal fascia and superior constrictor muscle are spread through to the glistening white prevertebral fascia. This bipedicle musculomucosal flap is elevated away from the prevertebral fascia with a right-angle scissors. One end of the flap is cut across, preserving either a superior or an inferior pedicle as desired. A superior pedicle was used in 16, and an inferior pedicle in 33 of the 49 patients operated on for speech defect by transfer of a pharyngeal flap to the posterior palate. A healthy section of superior constrictor muscle was included in all the flaps.

The authors describe a method of electromyographic evaluation of the muscular activity of the palatopharyngeal tissues. In all the pharyngeal flaps tested (superior pedicles and inferior pedicles), normal motor units were demonstrated. The palatal muscles were individually and simultaneously tested for comparative purposes. Similar electromyographic patterns in voltage, frequency, and wave form were noted in the pharyngeal flap as well as in normal tensor palatini, levator palatini, and the superior constrictor. On the basis of these studies it is felt that the pharyngeal flap is a dynamic muscular unit. Selective planning of the width, location, and position of the flap and its pedicle, as well as its point and extent of insertion, affords more suitable and wider application of the pharyngeal flap to anatomic defects and physiological paresis, as well as to cleft palate problems.

Symptomatology and Therapy of Bronchial Adenomas. H. Reitter. Ztschr. Tuberk. 112:257-272 (no. 5-6) 1959 (In German) [Leipzig, Germany].

The author reports on 8 male and 11 female patients, between the ages of 15 and 63 years, with bronchial adenoma who were admitted to the surgical clinic of the Medical Academy in Duesseldorf, Germany, between 1951 and 1958. These 19 cases of bronchial adenoma were observed among 1,800 cases of bronchial and pulmonary tumors in the last 10 years. In 11 of the 19 patients, the tumor was localized at the points of origin of the lobal bronchi; in 5, in the main bronchus; and in 3, in segmental bronchi. The duration of symptoms which preceded the diagnosis varied from 2 months to 30 years. The characteristic main symptoms during the first stage of the disease were recurrent hemoptyses and chronic, dry, irritative cough. These symptoms were observed in 16 of the 19 patients, and 13 of them had hemoptyses. The second stage of the disease was characterized by progressive bronchial stenosis with resulting atelectasis, chronic pneumonia, and abscesses; these secondary changes of the parenchyma, rather than the tumors as such, induced the patients to consult a physician. Early diagnosis is imperative in order to prevent such irreversible pulmonary changes. Although chest roentgenograms and tomograms may reveal the tumor in only 20% of the cases, the diagnosis of bronchial adenoma can be established with the aid of bronchoscopy and exploratory excision followed by microscopic examination.

Surgical treatment is the method of choice, and bronchoscopic removal of the tumor should be omitted because of the highly increased risk of recurrence. Eighteen of the 19 patients were operated on; one patient was not operated on because of amyloidosis. Of the 18 patients, 7 had lobectomies, 6 pneumonectomies, 3 segmental resections, and 2 bilobectomies. The local removal of the tumor by bronchotomy, resection of the bronchus, or segmental resection is rarely sufficient, and pneumonectomy and lobectomy are required in most patients because of secondary parenchymal damage. There were 2 operative deaths, representing a mortality rate of 11%. Two patients died within 2 months after the operation, and malignant changes occurred after one year in one patient. Fourteen patients obtained satisfactory results, and 2 had recurrences within 5 and 6 years after the operation. Careful postoperative control is required, since local occurrences are to be expected in 10% of the patients and malignant changes in an additional 10%. In case of recurrence, thoracotomy should be repeated with radical removal of the tumor. The prognosis of such a repeated operation is favorable. Metastases of bronchial adenomas are rare, but may occur with tumors of the carcinoid type. Metastases are not to be considered as contraindications to surgical treatment; solitary secondary tumors may be successfully removed surgically.

Some Observations Regarding 905 Patients Operated upon for Protruded Lumbar Intervertebral Disc. J. Raaf. Am. J. Surg. 97:388-399 (April) 1959 [New York].

Low-back and sciatic pain remains a complicated problem. To learn more about the results obtained with surgery, the author reviewed the case histories of 817 patients operated on by himself and of 88 patients operated on by his associates during the last 20 years for protruded lumbar intervertebral disk. A total of 954 operations for protruded disks were performed on these 905 patients. Protruded intervertebral disks were found in 76.2% of the 819 patients on whom the first operation for protruded disk was performed by the author or his associates; lesions about the nerve root other than disk protrusion were found in 5.5% of the patients; and no gross nerve root lesions could be found in the remaining 18.3%. Single protruded disks were found in 610 patients. Herniations of the nucleus pulposus were found in 558 of these 610 protrusions; 36 protrusions of the annulus were thought to be the cause of symptoms; and in 16 instances both annulus and nucleus pulposus were herniated. In 14 patients in whom 2 protrusions were found, 24 were herniations of the nucleus pulposus and 4 were protrusions of the annulus.

More than two-thirds of the patients were between the ages of 30 and 50 years. A fifth of the patients were women. About 70% of the patients gave a history of definite back injury. In comparing the symptoms, signs, and laboratory and roentgenologic findings in the 3 groups of patients, it was found that there were no significant differences between those with protruded disks, those with other nerve root lesions, or those without gross root lesions. However, a decrease in the achilles tendon reflex was found more often in patients with a protruded disk at the level of L-5 to S-1, and a decrease in the patellar reflex was found more often in those with protruded disks at the L-3 to L-4 space. Roentgenographic evidence of narrowing of a disk space could not be relied upon as evidence of a protruded disk.

Clinical judgment based on evaluation of the symptoms, signs, and laboratory and x-ray findings, exclusive of the Pantopaque test, was 82% accurate in making the diagnosis of protruded lumbar intervertebral disk. The Pantopaque test in 765 patients was proved to be 82% accurate. Clinical diagnosis and the Pantopaque test were simultaneously correct in 72% of 765 patients explored for protruded disk; both were incorrect in 7%; the clinical opinion was correct and the Pantopaque study incorrect in 11%; the Pantopaque study was correct and the clinical opinion incorrect in 10%. The over-all results of surgery in the patients operated on for protruded lumbar intervertebral disk were excellent in 43%, good in 37%, fair in 14%, and poor in 6%. In patients receiving compensation the results were claimed to be less satisfactory than in those not receiving a permanent partial disability award at the time their condition became stationary. The best results were obtained when a protruded disk was removed and no spinal fusion was deemed necessary. Surgical complications were few, and there were no operative deaths.

Complications of and Surgical Treatment for Primary Tuberculosis in Adults. P. Szigeti and M. Fráter. Ztschr. Tuberk. 113:12-19 (no. 1-2) 1959 (In German) [Leipzig, Germany].

A review of the literature on primary tuberculosis in adults and children and the authors' observations on adult patients with primary tuberculosis showed that complications of primary tuberculosis and the tendency of primary tuberculosis to progression occur more frequently in adults than in children. The authors have subdivided their adult patients with primary tuberculosis into 2 main groups. The first group consisted of patients with tuberculous lymphadenitis, the clinical aspect of which was predominated by enlargement of the bronchopulmonary lymph nodes. In this group were patients with segmental or lobal atelectasis which resulted from obstruction or perforation of an enlarged bronchopulmonary lymph node. The case of a 24-year-old woman with this form of primary tuberculosis is reported. On admission to the Johannis Hospital in Budapest, the patient's sputum was positive, and roentgenographic and bronchoscopic examinations revealed a compression stenosis of the Nelson type and atelectasis of the 6th segment. In the course of one year, during which the patient was hospitalized and was given antituberculous chemotherapy, the lymph node shrank, and the atelectasis subsided. This observation showed that regression of epituberculotic complications, which are caused by bronchopulmonary lymph nodes in adult patients, can be achieved by persistent administration of drugs, although it may be difficult and may take considerable time to exert an effect on the lymph node component.

The second group consisted of patients, whose primary tuberculosis was characterized by a complication in the peribronchial lymph node and in the parenchymal focus (primary complex). Two cases with complications of this type are reported. In the first, the bronchopulmonary lymph node perforated slowly into the bronchus, causing primary bronchogenous dissemination by way of a fistula, with resulting small and moderately sized foci in the lower lobe. The second case occurred in a 20-year-old woman a few weeks after delivery; the primary tuberculosis was resistant to drug therapy, and progression occurred in the peribronchial lymph node of the hilus and in the parenchymal component of the primary complex. To prevent further progression, total resection was carried out of the lymph node and of the 6th segment containing the parenchymal focus which showed irreparable fibrocaseous changes. Plastic surgery of the intermediate bronchus was done. Primary healing occurred, and the patient made a complete recovery. Surgical treatment thus can be successful in adult patients with primary tuberculosis resistant to drug therapy.

Intestinal Angina: Report of a Case with Preoperative Diagnosis and Surgical Relief. W. P. Mikkelsen and J. A. Zaro Jr. New England J. Med. 260:912-914 (April 30) 1959 [Boston].

The authors report on a 62-year-old man in whom for 2 years abdominal pain had occurred intermittently after meals, being occasionally associated with and relieved by vomiting. The pain was of a squeezing, bloating character and centered in the upper and right portions of the abdomen. Although it did not occur after every meal, a heavy meal was especially likely to precipitate it. Establishment of the correct diagnosis of "intestinal angina" (a term which most clearly identifies a syndrome of "work" intestinal ischemia which may, for months or years, precede complete occlusion of the mesenteric artery) was facilitated in this patient by the presence of advanced occlusive disease of the abdominal aorta. However, the "food-pain" relation was distinct. A weight loss of 50 lb. (22.7 kg.) had occurred. All laboratory tests and the usual x-ray studies yielded normal results.

At surgical intervention, complete abdominal exploration was negative in this patient, with the exception of the following vascular abnormalities. Occlusion of the abdominal aorta started at a level just below the renal arteries and extended to the external iliac arteries bilaterally. The inferior mesenteric artery was occluded. The superior mesenteric artery and its intestinal branches were pulseless; nor was a thrill palpable in this vessel or its branches. A thrill, though, was palpable in both the hepatic and the splenic arteries, but an expansile pulse was absent in both these vessels. Whereas ostial atherosclerosis existed, the principal cause of the obstruction of the superior mesenteric artery proved to be encasement of its first few centimeters by periaortic cicatrization. Successful liberation and endarterectomy of the superior mesenteric artery were carried out. During the 2 months after operation the patient gained 8 lb. (3.6 kg.) in weight, the symptoms of anginal pain were completely relieved, and postcibal distress completely disappeared. A longer postoperative follow-up will be required, though, to evaluate accurately this patient's response to the surgical treatment.

It is believed that the case of this patient is the first one in which the diagnosis of intestinal angina was recognized preoperatively and in which elective surgical treatment was successful. A heretofore unrecognized mechanism of impediment to the blood flow through the superior mesenteric artery was observed. Complete relief from the symptoms of intestinal pain followed surgical correction.

Treatment of Chronic Coronary Insufficiency with Bilateral Ligation of the Internal Mammary Artery. V. I. Kolesov, Y. N. Vishneevska, A. I. Drevina and E. A. Tsalolihhina. Vestnik khir. 82:33-41 (April) 1959 (In Russian) [Leningrad].

Animal experiments (on dogs) demonstrated that the internal mammary arteries anastomose with those of the pericardium and myocardium. Fifteen patients with coronary insufficiency of high degree were subjected to ligation of both internal mammary arteries. Most of these patients had suffered attacks of anginal pain for many years and were invalids. Nine of them had had a myocardial infarction, and 5 of them had it twice. Medical therapy failed to bring about any improvement. The follow-up of 10 of the 15 patients revealed that they were free from attacks of anginal pain or that they suffered from them rarely. The anginal pains were not as long lasting as they were previous to the operation. The conditions of 2 patients were not improved. Of the 13 patients who had good results, 12 remained improved, while one relapsed into the previous condition. The favorable clinical effect of the operation was corroborated by electrocardiographic changes which showed an improvement in coronary blood circulation.

Disseminated Lupus Erythematosus of the Alimentary Tract. J. Bruce and W. Sircus. Lancet 1:795-798 (April 18) 1959 [London].

The 27-year-old woman whose case is presented had 11 attacks of intestinal crises between May, 1955, and her death in April, 1958. During the first attack a presumptive diagnosis of appendicitis was made, and laparotomy was performed. The abdominal cavity contained about 3 pt. of clear yellow fluid. The small intestine was diffusely congested, and a few mesenteric nodes were enlarged. The appendix and other viscera appeared normal, but appendicectomy was carried out. Nausea and vomiting continued after the operation, and gastric aspiration and intravenous administration of fluid and electrolytes were needed. The temperature remained elevated (102 F), and an erythrocyte sedimentation rate (E. S. R.) of 65 mm. in one hour was noted. Intermittent pyrexia continued until discharge, and the E. S. R. remained at 100. Because of profuse diarrhea, central abdominal colic, and repeated vomiting, the patient was readmitted the day after discharge. The abdomen was distended and tender, and bowel sounds were absent. Vomiting continued, and hiccups and dehydration necessitated gastric suction and intravenous therapy. Examination with the aid of a barium meal showed coarse jejunal mucosa with irregular dilatation of the intestinal loops. Repeated blood cultures and fecal cultures were negative, and all serum agglutination reactions, including Brucella and Paul-Bunnell tests, were likewise negative.

A third attack shortly after discharge responded to drip and suction treatment. At a 4th attack about 6 months later, the uncertainty of the diagnosis and the severity of the attacks were considered to justify a laparotomy. Free fluid was again present in the abdominal cavity. The jejunum was grossly abnormal. The loops were heavy, intensely congested, and of a deep plum color. The mesentery was congested and edematous, and the mesenteric nodes were enlarged. Subserous ecchymoses appeared wherever the intestine was handled. The 5th attack of intestinal obstruction came 16 days later and was again severe enough to warrant admission. At later attacks swelling of the joints and mental symptoms appeared. Rubbery, enlarged nodes became palpable in the axillas and groins. Later liver function tests were found to be abnormal. During the 9th attack of intestinal obstruction, drip and suction therapy were again employed, and L. E. cells were now found in the peripheral blood.

At autopsy histological studies revealed acute and chronic vascular lesions of disseminated lupus erythematosus throughout the length of the alimentary tract.

Osler, in 1895, reported 11 cases of erythema exudativum multiforme, in all of which gastrointestinal crises—abdominal colics, usually with vomiting and diarrhea—were part of the disease. In the ensuing half century involvement of the digestive tract in disseminated lupus erythematosus, as the disease became known, was frequently noted, but little was known about the pathological basis of the alimentary symptoms. The authors feel that recurrent attacks of transient acute intestinal obstruction with segmental ileus in young subjects, especially women, with diarrhea accompanied by pyrexia and leukopenia, should suggest the diagnosis of intestinal lupus erythematosus, even in the absence of other recognizable phenomena of the systemic disease. At laparotomy, swollen, soggy, deeply injected lengths of small intestine are characteristic. The only difficulty in diagnosis—the differentiation between recurrent Crohn's disease and jejunitis acuta—may be resolved by observing the transient nature of the attacks, with either spontaneous resolution or rapid improvement on treatment with steroids or antihistamines.

Experience with Gastric Resection by the Péan-Rydygier-Billroth I Method. E. Polák and Vojtíšek. Ann. Surg. 149:475-480 (April) 1959 [Philadelphia].

The authors cite the merits of the gastric resection methods of the Polish surgeon, Rydygier, and the Czech surgeon, Jedlička, as treatment for gastroduodenal ulcer. Rydygier was the first surgeon to resect a stomach for stenotic pyloric ulcer, and Jedlička provided the first extensive statistics showing 3% mortality. The authors prefer the Péan-Rydygier method of resection on the basis of more than 30 years' experience. This method, in which the duodenum along the greater curvature is anastomosed to the stomach, seems to give the best results and is no more difficult than the Billroth II method, if the ulcer is removed.

The authors studied the occurrence and the significance of recurrence of ulcers in patients operated on at the surgical clinic of the Medical Faculty of Hygiene in Prague over a period of 20 years. After the original resection by the Péan-Rydygier method there were 0.65% recurrences; after the Billroth II resection, 0.4%; and after palliative resection without excision of the ulcer, 1.4%. Although it seems easier to perform operative correction after the Péan-Rydygier resection than after the Billroth II resection, the former resection also has its contraindications when the necessary conditions are not present for the possibility of end-to-end anastomosis. The chief contraindications are as follows: 1. The duodenum is not suitable for anastomosis because it is scarred or altered by a deeply penetrating and large ulcer on the posterior wall. 2. The position of the ulcer, with fixed cardia and immobile duodenum, is too high, so that suture cannot be made without tension. However, gaining a sufficiently large duodenal stump depends to a certain degree on the experience of the operating surgeon; the more experienced he is, the more rarely must he turn to a blind closure of the duodenum. The second contraindication is even more relative. Usually it is possible to leave a sufficiently large stump along the greater curvature, and the duodenum can be easily mobilized after incision of the peritoneum along the lateral wall pars descendens duodeni, so that suture end to end can be made without tension.

The individual listing of operations made by the senior author of this paper during the last 3 years was compared with those performed by all other surgeons at the clinic. This surgeon has achieved 90% operability with the Péan-Rydygier method, the mortality being under 1%. His co-workers have achieved 78% operability, the mortality being 1.5% *with the Péan-Rydygier method. The over-all mortality* among patients operated on by all members of the clinic staff, using both methods, was 1.9% during the last 3 years; there were 25 resections for perforated ulcer, 10 operations for massive hemorrhage, and 9 procedures for recurrence of ulcer. This shows that resection with gastrojejunal anastomosis can be limited, and at the same time the mortality rate can be kept down to less than 1%.

Late Results of Vagotomy in Ulcer Disease of Stomach and Duodenum. A. N. Filatov and E. A. Senchillo. Vestnik khir. 82:50-55 (April) 1959 (In Russian) [Leningrad].

The authors report on 64 patients with gastric and duodenal ulcers who were treated by vagotomy. Sixty patients were followed up. Thirty-eight of these were subjected to a subdiaphragmatic vagotomy. Nineteen patients were subjected to a vagotomy and a gastroenterostomy. Forty-seven patients were followed up for from 2½ to 10 years. The follow-up demonstrated that half of the pa*tients became worse as time went on. Best results* were noted in cases of peptic ulcer and in ulcers of the pylorus when vagotomy was combined with gastroenterostomy. The authors feel that a favorable result depends on the complete severance of all branches of the vagus and on proper evacuation of the gastric contents furnished by the gastroenterostomy. They feel that vagotomy may be recommended for gastric ulcers located high up in the fundus and for duodenal ulcers with a difficult approach. Its main indication is recurrence of ulcer disease after gastric resection.

Strangulated Obturator Hernia. U. Muraro. Riforma med. 73:332-336 (March 21) 1959 (In Italian) [Naples].

A successful operative case of strangulated obturator hernia in a 73-year-old woman is presented. The patient had had a crural hernia for 20 years without noticing any symptoms of strangulation. The author believes that in such a type of hernia the problem is more of a diagnostic nature than of an operative nature. Mild symptoms and signs, such as pain in the internal surface of the radix of the thigh, swelling noticed on examination of the rectum or the vagina, or a marked sensibility of Scarpa's triangle, are important in the diagnosis of strangulated obturator hernia. This type of hernia should be suspected especially in cases of intestinal occlusion. Intervention through the abdomen is the treatment of choice; in case this is not sufficient a femoral incision is of help. Exceptionally and only in case of a large hernia which goes to the root of the thigh should intervention begin through the thigh. The author lays emphasis on the fact that, when the diagnosis of strangulated obturator hernia is made, or when this condition is suspected, a median subumbilical laparotomy, with the patient *in an exaggerated Trendelenburg position,* affords a good approach and a clear view of the operative area.

Spontaneous Perforation of the Stomach in the Newborn: Analysis of Thirteen Cases. L. M. Linkner and C. D. Benson. Ann. Surg. 149:525-533 (April) 1959 [Philadelphia].

The authors report on 13 newborn (4 male and 9 female) infants operated on for spontaneous rupture of the stomach at the Children's Hospital of Detroit during the last 10 years. It was hoped that similarities would become apparent to establish a common etiology and a common clinical picture, which should lead to earlier correct diagnosis and, consequently, to a higher salvage of these newborn infants. The commonest symptoms were marked abdominal distention of sudden onset, vomiting, and a tympanitic abdomen. Roentgenologic examination usually revealed a large amount of free air and fluid in the peritoneal cavity or beneath the leaves of the diaphragm. The infants were then im*mediately prepared for operation. A right para*median incision or an incision through the upper midline was made. Postoperatively, continuous suction was employed until intestinal sounds were heard or stools passed. This normally occurred between 36 and 48 hours after the operation. Oral feedings by eye dropper of glucose solution every hour in 2-cc. amounts were then started and gradually increased in volume. Six of the 13 children survived.

It would seem from those surviving that a delay of more than 12 hours from perforation to surgical correction is often fatal. It is evident that survival was related directly to the promptness with which roentgenologic examination of the abdomen was made and surgical correction of the defect accomplished. Many factors have been postulated to explain the pathogenesis of this condition, but review of the site of perforation has provided no clue to the etiology. All areas of the stomach were involved with almost equal frequency, but the posterior gastric wall was involved least frequently. Pregnancy, labor, and delivery were usually normal; however, in the mothers of 2 patients toxemia was noted. Weight had little to do with the ultimate survival. An additional point that might indicate a common pathogenesis was the incidence of positive blood cultures in 3 patients. It can be postulated that septic embolization of the gastric wall might produce a local vascular insult sufficient to allow the highly acid gastric juice of the newborn *infant* to perforate through all the layers.

Subclinical or Latent Adrenal Insufficiencies. L. De Gennes, H. Bricaire and L. Moreau. Presse méd. 67:619-622 (March 28) 1959 (In French) [Paris].

Subclinical or latent adrenal insufficiency may exist even though the clinical signs suggestive of such a condition are almost indistinguishable or entirely lacking. Any unusual strain on the organism, such as an intercurrent infection or the shock of an operation, may then overtax the adrenal glands, precipitating an episode of acute insufficiency and endangering life. Investigation of the adrenal function in 10 patients in whom latent adrenal insufficiency was revealed by stress produced 2 different types of findings: (1) low static values of the steroids with a normal or slight increase in response to ACTH stimulation, and (2) normal or slightly lowered steroid values with no response to ACTH stimulation. Findings of the first type reveal a disturbance of the gland not infrequently seen in hypopituitarism, after prolonged corticotherapy, in connection with muscular inactivity in bed-fast patients, in psychasthenia, and in active visceral tuberculosis.

The adrenal inertia revealed by findings of the second type is undoubtedly due to partial but definitive impairment of the adrenal glands. Surgical procedures, especially shock-producing operations such as thoracoplasty and pneumoperitoneum, are not without danger in patients with adrenal inertia and may be followed by collapse related to the slowness of the adrenocortical response. It must be remembered that lowered urinary steroid values are not necessary for a diagnosis of adrenal insufficiency in these cases; repeated tests may show normal or only slightly lowered values, but in all cases the Thorn test fails to produce an increase. Clinical signs, such as asthenia, loss of weight, and pigmentation, often exist but may be so slight as to escape observation unless deliberately looked for; they were present in 6 of the authors' 10 patients.

Latent or subclinical adrenal insufficiencies of the kind described almost always represent incipient Addison's disease in which the glandular secretion is active enough to meet everyday needs but is quite incapable of responding to those created by a major stress. Collapse in most of the authors' patients was followed by an intensification of the Addisonian signs. Adequate hormone treatment will restore the balance in most cases and can sometimes be discontinued after the patient's recovery from the acute attack. Patients should be warned, however, that in the event of even slight shock they are to be regarded as adrenally inadequate and must be treated accordingly. The true status of the adrenal gland should also be investigated before every operation, so that prophylactic therapy can be given before, during, and after the operation when needed. This procedure, which has been adopted by some surgeons at the authors' suggestion, seems already to have borne fruit and to have brought about a reduction in postoperative mortality attributable to acute adrenal insufficiency.

Primary and "Accelerated" Early Plastic Surgery for Burns. G. Frank. Plast. & Reconstruct. Surg. 23:313-330 (April) 1959 [Baltimore].

The author describes the efforts made at the Municipal Hospital in Budapest, Hungary, to shorten the time between the burn accident and its surgical treatment. He emphasizes the importance of terminology in regard to the time elapsed between the burn accident and the treatment. He differentiates between primary and secondary operations. A primary operation should be understood to mean necrectomy and closure of the wound within 48 hours after the accident. The essential difference between primary and secondary management lies in infection and in the development of an inflammatory barrier. The term "late plastic repair" applies to the correction of scar formation and of defects. In the group of primary operations the author distinguishes between "immediate" and "delayed" primary necrectomy and grafting. Immediate primary operation is the one performed within 12 hours, and delayed primary operation is that carried out within 48 hours after the burn. In the group of secondary operations a distinction is made between "accelerated early," "retarded early," and "overdue" grafting. Accelerated early operations are the ones performed within 3 to 14 days after the accident, whereas during the ensuing 4 to 6 weeks the retarded early operations are performed.

This report is concerned with the techniques employed and the experience obtained in 43 cases of primary and 16 cases of accelerated early plastic operations for deep burns. In the conclusions the author emphasizes the following points: 1. When it is certain that a burn involving less than 2% of the body surface is deep, primary necrectomy and immediate wound closure (suture and covering by flap or graft) are indicated. 2. When an extensive burn is deep, the shock due to burn is no contraindication to operation within the first 48 hours, because tolerance can be enhanced by supporting the usual antishock measures by pharmacological hibernation by means of the lytic cocktail (in burns involving up to 10 to 15% of the body surface), or by hibernation and hypothermia (in burns more extensive than that). Surgical shock can be combatted, and meanwhile the burn shock will be over, too. 3. Grafts will take, even if the body temperature has been reduced to as low as 28 C (82.4 F), and epithelization will result. 4. Primary surgery is contraindicated when (*a*) the deep burn involves more than 30 to 40% of the body surface; (*b*) the deep burn is smaller than that but affects also the principal donor areas; (*c*) the necrotic skin cannot be removed completely (more than 5% of body surface remains necrotic); and (*d*) the trunk is deeply burned circularly, because in such cases only one aspect (anterior or posterior) of the body can be operated on. 5. When the principal donor areas are involved, primary homografting may be employed after necrectomy. 6. Only those burns should be excised in which there is no chance that epithelial regeneration may begin from the wound floor. 7. A deep burn in the center of a superficial one can be excised and grafted with success. 8. At necrectomy each part of the wound base should be examined for bleeding. 9. In extensive necrectomy the electrodermatome or Lagrot's or Humby's knives are the instruments of choice. 10. Only coagulation necrosis is suitable for accelerated early plastic surgery (necrectomy plus immediate grafting, performed within 3 to 14 days after accident). In colliquative necrosis it is advisable to be more conservative, and the rules of delayed early grafting (2 to 6 weeks) should be applied.

The Importance of Cholangiography on the Operating Table. B. A. Petrov and V. B. Antonovich. Khirurgiya 35:16-20 (no. 4) 1959 (In Russian) [Moscow].

The authors report on 150 patients with calculous disease of the gallbladder and the bile ducts who were subjected to cholangiography in the course of operation. In 44 out of 113 patients with stones in the gallbladder, the common bile duct was demonstrated to have stones in it. Jaundice was present in only 24 of the 44 patients; stones were palpated in the common bile duct in 25; and in 16 stones were demonstrated only by cholangiography.

Cancer Cells in the Blood: A Five to Nine Year Follow-up Study. H. C. Engell. Ann. Surg. 149:457-461 (April) 1959 [Philadelphia].

Blood samples from 125 patients with cancer, most of whom had intestinal carcinomas, were examined for tumor cells. Samples were drawn from the tumor area and from peripheral blood during operation for removal of the primary growth. Tumor cells were found in 34% of the grade 2 tumors, in 76% of the grade 3 tumors, and in 100% of the grade 4 tumors. The assumption that a certain number of patients, on whom radical operation had been performed and who had tumor cells in the blood, would survive a 5-year period has been confirmed by a 5-to-9-year follow-up study of the patients. Of the 125 patients, 55 were alive after 5 to 9 years. Tumor cells were found in the blood of 76 of the 125 patients. Of the 55 surviving patients, 28 had cancer cells in their blood at the time of operation. In the vast majority of these patients all tumor cells disseminated into the blood must have perished in the blood stream. This illustrates that no prognostic conclusion can be drawn from the appearance of tumor cells in the blood. The presence of such cells in the blood during surgical resection of a tumor area has been found to be related, primarily, to histological differentiation of the tumor, and, to a less degree, to local extension, while surgical trauma seems to be of little consequence in venous spread of cancer cells from colonic and rectal carcinomas. Operative trauma plays a minor role in patients with intestinal carcinomas.

The Role of Surgery in the Management of Unilateral Pleural Effusion. T. B. Ferguson and T. H. Burford. Ann. Int. Med. 50:981-998 (April) 1959 [Lancaster, Pa.].

The most common causes of persistent unilateral pleural effusion are tuberculosis, metastatic carcinoma, and heart failure, but a variety of other disease processes can give rise to such fluid collections. Determination of the etiology of such an effusion may prove difficult. One of the authors (T. H. B.) has been of the opinion that major exploratory thoracotomy should be done in patients of this type in whom the diagnosis cannot be obtained by any of the usual methods. The advantages of major thoracotomy are several. Tissue can be obtained for histological and bacteriological study with the certainty that the biopsy is representative. Decortication of the compressed lung can be done when necessary, and, if dyspnea due to rapid reaccumulation of fluid is a problem, this complication can be controlled by obliterating the pleural space with a parietal pleurectomy. If an active tuberculous process is found, the patient can then be placed on bed rest and antituberculous therapy. If a malignant lesion is present, palliation can be achieved by relieving the dyspnea caused by fluid accumulation.

The authors present observations on 21 patients with persistent unilateral pleural effusion, whom they observed during the last 7 years. The average age of the patients was 51 years, and the group included 16 males and 5 females. Fluid accumulation had persisted for an average of 3½ months. The effusion contained gross blood in 7 of the 21 patients. After the usual diagnostic methods had failed, all the patients were subjected to elective exploratory thoracotomy. Only 3 patients proved to have malignant disease at operation. Of the remaining 18 patients, 6 had tuberculous pleuritis, and 12 had nonspecific inflammation of the pleura. The presence of blood in the effusion was of no help in determining whether the causative process was neoplastic or inflammatory. Of the 7 patients with a bloody effusion, 1 had cancer, and 6 had inflammatory disease. All the patients derived therapeutic benefit from operation. Restoration of lung function was accomplished by decortication when a constricting membrane was present. Fluid reaccumulation was permanently abolished by performing a total parietal pleurectomy. Sixteen of the 21 patients are clinically well more than 3 years after operation, including 6 patients with active tuberculosis of the pleura. The authors conclude that exploratory thoracotomy with pleural biopsy, decortication, and parietal pleurectomy should become an integral part of the management of every patient who has a persistent undiagnosed unilateral effusion.

Coarctatio Aortae Abdominalis. A. L. D'Abreu, C. G. Rob and J. F. Vollmar. Arch. klin. Chir. 290: 521-546 (no. 6) 1959 (In German) [Berlin].

The authors report on a 58-year-old woman and on a 40-year-old man with coarctation of the abdominal aorta, who were operated on in the surgical departments of St. Mary's Hospital in London and the Queen Elizabeth Hospital in Birmingham, England, during 1957-1958. The woman had a segmental coarctation of the abdominal aorta with localization below the origin of the renal arteries. Signs of intermittent claudication predominated in the clinical picture. The onset of symptoms occurred when the patient was 40 years old. For 6 years an erroneous diagnosis of multiple sclerosis was maintained, and later an erroneous diagnosis of thrombosis of the aorta was made. High lumbar aortography revealed coarctation of the aorta. Considerable improvement of the blood circulation in the lower portion of the body resulted from a splenoaortic bypass operation with insertion of a homologous arterial graft. Coarctation of an unusually long segment of the abdominal aorta of the "deep"-thoracicoabdominal type was found in the man. Hypertension of 15 years' duration, representing the clinical guiding symptom, had been treated unsuccessfully with drugs and by thoracolumbar sympathectomy. Symptoms of intermittent claudication were present for the last 5 years. Resection of a constricted area of about 20 cm. in length could not be considered because of its location. An almost complete cure of the deficient circulation of the caudal portion of the body and of the hyptertension of the upper portion of the body resulted from an aortoaortic bypass. Twenty-two additional cases of coarctation of the abdominal aorta in 11 men and 11 women, of the average age of 34.2 years at the time the clinical diagnosis was made, were collected from the literature.

The following types of coarctation of the abdominal aorta may be distinguished from the morphologic viewpoint and from that of localization: (1) segmental and hypoplastic type and (2) infrarenal, intrarenal, and suprarenal type. The close topographic relationship of most of the forms of coarctation with the renal arteries may result not too rarely in a partial or complete occlusion of these arteries. The clinical picture, as a rule, is predominated by the signs of deficient arterial circulation of the lower portion of the body (intermittent claudication of the legs), and less frequently by hypertension of the upper half of the body or by signs of an overload placed on the heart. The diagnosis is supported primarily by the demonstration of a deep (thoracicoabdominal) collateral circulation (pulsating vessels at the borderline of the thorax and abdomen, bone erosion at the lowest ribs, vascular sounds in the course of the abdominal aorta and at the back). The diagnosis of the vascular narrowing can be established by aortography. Thrombosis of the aorta and essential or renal hypertension are the most frequently made erroneous diagnoses. Direct operative removal of the coarctation is indicated only in patients with short constricted segments, which are cranial or caudal of the "critical" zone of origin of the large visceral arteries. A bypass operation is to be preferred for coarctation in the "critical" zone. Sympathectomy should be limited to cases of the hypoplastic type; it is a purely palliative measure, and its results in patients with coarctation of the abdominal aorta were disappointing.

Disability Following Gastric Surgery for Benign Disease, as Observed by the Internist. E. D. Palmer. Ann. Int. Med. 50:928-935 (April) 1959 [Lancaster, Pa.].

This report deals with 157 patients who had had a stomach operation for benign disease, and who subsequently either consulted a medical outpatient clinic or were referred to a medical hospital ward. In 83 instances the operation had been a Billroth 2 subtotal gastrectomy; in 40, vagotomy and gastroenterostomy; in 29, simple gastroenterostomy; and in 5, total gastrectomy. The operations had been done by many surgeons in many hospitals. No effort was made to evaluate the effectiveness of different operative procedures. All the patients were hospitalized for at least part of the study. In addition to the usual clinical evaluation, they were studied by periodic upper gastrointestinal roentgenography and gastroscopy. The patients who had undergone total gastrectomy were examined by esophagoscopy and by jejunoscopy. Thirty-two of the other patients were also studied esophagoscopically.

In 56% of the patients, an organic postoperative complication was found, with or without additional functional problems, and in many of them a new set of symptoms had replaced the preoperative ones, often a long period after surgery. In the other 44%, the symptoms were judged to have a nonorganic basis. Except for the 29 patients who had been treated by simple gastroenterostomy, and in 23 of whom organic causes were found, the causes of the disability were rather evenly divided between the organic and the nonorganic. Many of the patients in whom a specific organic diagnosis was possible also had nonorganic problems, both physiological and emotional. Forty-three of the patients came to medical attention because of upper gastrointestinal hemorrhage. These included all the patients in whom erosive esophagitis and gastritis were diagnosed during active bleeding by esophagogastroscopy. Anastomotic ulcer, gastric ulcer at a distance from the stoma, and active duodenal ulcer accounted for the hemorrhage in most of the others.

No cause was found in 7 patients who could not be examined until bleeding had stopped for some time. One of the more interesting causes of bleeding was adenoma of the jejunum, arising just below the stoma; this was discovered in 3 patients who had had subtotal gastrectomy. They were treated by local excision with revision of the stoma. Gastric carcinoma eventually developed in 2 patients who had been operated on for duodenal ulcer. In one of them symptoms leading to the discovery of cancer began 26 years after subtotal gastrectomy. The other patient had had a vagotomy and gastroenterostomy 8 years previously.

The most significant feature of the group without organic disease was that all but 4 of the 69 patients had been operated on because of duodenal ulcer and that only 3 of these had had an organic ulcer complication. Complaints in this group included the dumping syndrome, or anorexia, nausea, vomiting, weight loss, diarrhea, and fainting in various combinations. The most difficult group was composed of 30 patients who just had not felt well since operation. They never seemed sure of how they had changed. They did not feel the way they had before, but neither did they feel the way they thought they should now. Some seemed to have undergone an emotional change. They seemed to be abnormally dependent on both medical and family figures in a compulsive sort of way, sometimes but not regularly using the fact of their operation to manipulate their surroundings. Additional surgery was carried out in 48 of the 157 patients, and 2 were subjected to esophageal dilatation. The others, including those with nonorganic lesions, were treated by conservative medical measures and by interview therapy.

Modification of Blood Clotting Abnormalities by Splenectomy in Chronic Idiopathic Thrombocytopenia. G. Winckelmann. Ztschr. klin. Med. 155:536-543 (no. 6) 1959 (In German) [Berlin].

The author studied the influence of splenectomy on the processes involved in blood coagulation in 10 patients (9 women and 1 man) with idiopathic thrombocytopenic purpura. Particular attention was given to the maximal retractility of the clot in the graph illustrating the clotting process, the consumption of prothrombin, and the thrombocyte count after splenectomy. After a successful splenectomy there occurred within 6 hours, despite only a minor increase in thrombocytes, a noticeable increase in the density of the clot and a growing consumption of prothrombin, that is, the platelet function was increased. The prompt postoperative onset of the emergence of functionally adequate thrombocytes into the circulating blood was attributed to the abolishment of a splenogenic inhibitory effect on the bone marrow. In addition, the favorable hemostatic effect of splenectomy even in the presence of a low thrombocyte count indicated a favorable modification of the vascular factor. In 6 patients the splenectomy achieved complete improvement of their defect, with normalization of the thrombocyte count, of the changed coagulation process, as well as permanent improvement in the clinical symptoms. In one patient the bleeding tendency disappeared coincidentally with normalization of the capillary resistance and of the bleeding time, whereas the thrombocyte count and the disturbances in coagulation remained unchanged. In the remaining 3 patients splenectomy was followed by only a slight improvement in the hemorrhagic diathesis.

NEUROLOGY & PSYCHIATRY

Twenty-Six Cases of Atherosclerotic Obstruction of the Sylvian Artery. T. Alajouanine, P. Castaigne, F. Lhermitte and others. Semaine hôp. Paris 35: 1145-1149 (March 28) 1959 (In French) [Paris].

Obstructive atherosclerosis of the sylvian (middle cerebral) artery is one of the most frequent and recognized causes of softening in the region of the sylvian artery, but the arterial lesions and their connection with the cerebral necrosis are by no means well known. Special interest, therefore, attaches to the findings in 26 cases in which atherosclerotic obstruction of the sylvian artery was demonstrated by arteriography, because they make it possible to relate the clinical picture to the site of the obstruction. The anatomic and clinical correlations thus established help to clarify the physiopathology of the circulatory disturbances.

Classification of the atherosclerotic obstructions according to their position in the arterial trunk revealed 3 principal groups: (1) those occurring at the origin, which deprive the whole of the artery. including its perforators, of normal blood supply; (2) those at the threshold of the insula, where the arteries of the cortical and subcortical territory originate: among these, only the anterior temporal, already detached from the trunk of the sylvian, can escape the consequences of the obstruction; and (3) those at the origin of the trunk of the ascending arteries, on which the irrigation of the frontal and parietal convolutions largely depends.

The onset of the symptoms was almost always abrupt (23 cases), but loss of consciousness was comparatively rare (4 cases). A rapidly progressive development, within a few hours, of major disorders was much less common, having been observed only twice. A most unusual onset, finally, was seen in 2 patients in whom the disturbances increased little by little over a period of months. Premonitory signs, reported in nearly half the cases, consisted of paresis in 2; transient but always recurring paresthesias, lasting for minutes or hours, in 5; critical sensory or motor phenomena in 2; and headache in 3. These signs preceded the stroke by only a few days in 2 cases, but more often they revealed the development of the arterial process for months or even years before the onset of hemiplegia.

Hemiplegia and aphasia are the characteristic disturbances of cerebral softening due to obstruction of the sylvian artery, but they vary greatly in intensity. Different clinical pictures may, therefore, be produced by obstructions in one site, and, at the same time, the pictures produced by obstructions in several different sites may be identical. It follows, then, that some intermediate factor capable of explaining the variability of the circulatory deficit and its regular predominance in the same regions of the brain must intervene between the obstruction of the artery and the development of ischemia. This factor is to be found in the variability of the collateral circulation, which is supplied by meningeal anastomoses differing widely in their effectiveness and in the conditions under which they are brought into play. The insufficiency of the meningeal anastomotic networks also explains why cerebral softening due to obstruction of the sylvian artery is much more stereotyped in its expression and also, on the whole, much more serious than that caused by obstruction of the internal carotid artery, the consequences of which depend largely on the ability of the circle of Willis to provide collateral circulation.

Arteriographic studies in 86 patients in whom cerebral vascular accidents had occurred showed that one-third were due to obstruction of the sylvian artery, one-third to obstruction of the internal carotid artery, and one-third to undetermined causes. Arterial bifurcations are known to be an elective site for atherosclerotic lesions, and it is interesting in this connection to note the close anatomic similarity between the internal carotid and the sylvian arteries at their points of origin. Both arteries continue in the direction of the vessels from which they take their origin, and both receive the greater share of the blood carried by the parent vessel. The external carotid and the anterior cerebral arteries, on the other hand, receive the smaller share and branch off at a definite angle. The similarity of the morphologic and hemodynamic conditions at these 2 points of bifurcation in the arterial system inevitably invites comparison with the similarity of the lesions to which they are subject.

Bilateral Obstruction of the Internal Carotid. T. Alajouanine, P. Castaigne, F. Lhermitte and others. Semaine hôp. Paris 35:1149-1160 (March 28) 1959 (In French) [Paris].

The clinical and anatomic findings obtained in studying 5 patients with bilateral obstruction of the internal carotid arteries clearly revealed the importance of the collateral circulation in determining the effect of such an obstruction on the cerebral circulation. Complete suppression of the arterial supply of the internal carotid does not necessarily lead to necrosis of the whole of the parenchyma supplied by the middle and anterior cerebral arteries. Arteriographic studies made by the authors in 3 of their 5 patients show that partial reestablishment of the circulation takes place by way of the ophthalmic artery, the posterior communicating arteries, and perhaps the superficial anastomoses. Intermediate conditions of every kind are to be found between the cases in which the inadequacy of the collaterals makes bilateral carotid obstruction a fatal accident and those in which the collateral vessels are able to satisfy the requirements of the cerebral circulation.

The manifestations that characterize bilateral, as well as all other forms of cerebral arterial obstruction are linked to many other imperfectly understood factors. A few points, however, may be noted. 1. Collaterals adapt themselves to the new conditions created by the obstruction of a vessel, and the more slowly the obstruction develops, the better the adaptation. This fact was illustrated by the severity and abrupt onset of 2 cerebral accidents due to emboli in one of the patients, who had complex heart disease, as compared with the long history of transient disturbances presented by 2 other patients who had atherosclerotic thromboses, one of whom is leading a normal life in spite of the bilateral obstruction, while the other lived for a fairly long time (2 years and 3 months), although he had an occlusion of the vertebral artery as well as bilateral obstruction of the internal carotid arteries. 2. All parts of the brain are not equally exposed to the danger of ischemia by obstruction of the internal carotid arteries, but too many variables are involved to permit the formulation of a general rule. It was noteworthy, however, that in the 3 cases in which an autopsy was performed, the region of the sylvian artery was the site of important lesions, while the regions of the anterior and posterior cerebral arteries were only slightly or not at all affected. This is readily understandable in the case of the posterior cerebral artery but not so easy to explain in the case of the anterior cerebral artery. This unequal distribution of the lesions results from the anatomic and hemodynamic conditions governing the new organization of the circulation. Some of these are connected with the fact that the flow in the sylvian artery is greater than the flow in the anterior cerebral, so that, with a lessened arterial supply, the territory supplied by the latter vessel will be the one more easily irrigated; others depend on the capacities of the 3 components of the anastomotic network. A contrast medium injected into the ophthalmic artery after bilateral obstruction of the internal carotids, for example, enters the anterior cerebral in preference to the sylvian artery, whereas after unilateral obstruction the anterior cerebral is regularly injected by way of the contralateral carotid artery. The vast territory of the sylvian artery may be revascularized by the posterior communicating artery, but the fact that this vessel is often reduced in caliber readily explains its inadequacy as a collateral. The superficial networks participate, of course, in the work of revascularization, but their capacity is limited. Circulatory inequalities leading to varying degrees of necrosis are also to be found within the sylvian region itself. The clinical characteristics and course of the manifestations of bilateral obstruction of the internal carotid arteries thus depend on the intensity, duration, and site of the ischemia to which it gives rise.

The Cerebral Arteritis of Bacterial Endocarditis: Its Late Complications. T. Alajouanine, P. Castaigne, F. Lhermitte and J. Cambier. Semaine hôp. Paris 35:1160-1165 (March 28) 1959 (In French) [Paris].

Cerebral accidents in patients with bacterial endocarditis may occur at any time during the course of the disease or months or even years later. They are almost always the result of an arterial process ending in cerebral softening or a cerebral or meningeal hemorrhage. Hemiplegia is the commonest clinical expression of such an accident. Clinical, arteriographic, and biological data obtained in 3 personal cases serve to define the nature of the arterial lesion, the mechanism of the accidents it engenders, and its future after the subsidence of the infection. The first patient was a 33-year-old man in whom hemiplegia on the right side, accompanied by aphasia, appeared at the beginning of an attack of bacterial endocarditis due to a streptococcus of the viridans group. The cardiac infection responded rapidly to treatment with antibiotics, but the hemiplegia and aphasia showed little improvement. Two arteriograms of the left carotid artery, one taken during the initial phase of the hemiplegia and one 3 months later, revealed an aneurysm at the end of the left internal carotid and obstruction of this segment of the artery. A cerebrospinal fluid specimen obtained on the third day of the illness contained 2,500 cells per cubic centimeter, 95% of which were polymorphonuclear leukocytes.

The second patient was a 20-year-old youth who was suddenly affected by a predominantly brachiofacial hemiplegia on the left side 5 months after the clinical and biological cure of an attack of bacterial endocarditis unaccompanied by neurological signs of any kind. Arteriography revealed a narrowing of the last 2 cm. of the carotid, with an obstruction blocking the openings of the middle and anterior cerebral arteries and, finally, a calcification situated at the level of the obstruction. The cerebrospinal fluid contained 700 cells (80% lymphocytes) per cubic centimeter. No signs were found to indicate a resumption of the endocarditic process.

The third patient was a 47-year-old man with aortic insufficiency of rheumatic origin, who recovered completely from an attack of bacterial endocarditis after having been treated with penicillin for one month. Two years later a left-sided hemiplegia appeared abruptly during exposure to severe cold weather. Serious sequelae developed, and 18 months later the patient was hospitalized at the Clinique des Maladies du Système Nerveux, Paris, so that he could be given reeducative therapy for motor and speech disturbances. Arteriography of the right carotid revealed complete obstruction at the origin of the sylvian artery and a small aneurysm at the bifurcation of the internal carotid.

The cerebral accident in each of these 3 cases was undeniably softening produced by an obstruction at the junction of the carotid and sylvian arteries. The circumstances in which it became manifest, however, and the findings on arteriographic examination of the patients contribute to an understanding of the arteritis accompanying bacterial endocarditis. The arteriographic pictures leave no doubt that the lesion responsible for the cerebral disturbances consists of a focal injury to the arterial wall and the changes occasioned thereby. The processes illustrated—narrowing of the lumen of the carotid, arterial obstruction, aneurysmal dilatation, intraparietal calcification—evoke those already familiar in the arteries of the limbs and other territories of the body—inflammatory infiltration and alteration of the vessel wall ending either in obstruction or aneurysmal dilatation. The interval between the cure of the endocarditis and the occurrence of the cerebral accident in the last 2 patients (5 months and 2 years, respectively) seems to show that inapparent lesions may become established in the carotid and sylvian arteries during the course of bacterial endocarditis and that they may continue to develop independently after the endocarditis has been cured. The inflammatory reaction in the cerebrospinal fluid of the first 2 patients suggests either the latent development or the reawakening of arteritic foci. The location of the arterial lesions at the bifurcation of the internal carotid can perhaps be explained by the hemodynamic conditions found in that region. These conditions are known to be a determining factor in the localization of atheroma and the elective localization of sylvian thromboses. It may be noted that aneurysms of the cerebral arterioles can only reveal themselves by rupture, whereas accidents of ischemic necrosis, such as those reported by the authors, imply the obstruction of a major arterial trunk. This may explain the heretofore classic distinction made between aneurysms, which were attributed to arteritis, and obstructions, for which embolism was considered responsible.

Cerebral Atrophy Associated with Boxing. K. T. Neubuerger, D. W. Sinton and J. Denst. A. M. A. Arch. Neurol. & Psychiat. 81:403-408 (April) 1959 [Chicago].

While neuropsychiatric complications in boxers are well known, few reports have been published on the cerebral pathological aspects, particularly with regard to the late sequelae. The authors made studies on 2 patients with dementia pugilistica. Cerebral cortical biopsy in one patient revealed mild neuronal degeneration and definite plasmatic gliosis in the lower cortex. The brain of the other patient was severely atrophic, presenting a picture which grossly and microscopically resembled presenile brain atrophy (Pick's disease). As in other cases, the disease became manifest some years after cessation of professional boxing. The authors compare observations on their patients with descriptions of the pathological aspect of dementia pugilistica given by German investigators, who felt that the term "dementia pugilistica" should be reserved for cases of chronic progressive disorders developing after a symptom-free interval, and that neurological disturbances arising in immediate connection with head injuries should be called "traumatic encephalopathy of boxers." While the 2 cases presented have failed to reveal argentophilic changes, undoubtedly they belong in the group of senile and presenile cerebral involutions (senile brain atrophy, Pick's and Alzheimer's diseases). The mechanism of involution is understood best with the help of von Braunmühl's theory on the process of aging of the colloids of the brain. This process is characterized by diminution in the degree of dispersity of the colloids and by the separation of the medium of dispersion into 2 phases of different colloidal content, one of which consists of concentrated colloid with little water, and the other of a thin, watery medium with little colloid.

The authors feel that the pathogenesis of the traumatic lesions in their cases may be explained in accordance with the views of Brandenburg and Hallervorden and of Grahmann and Ule, which were predicated on von Braunmühl's theory. These authors believed that the cerebral alterations are thixotropic in origin. [Thixotropy, a term used in colloid chemistry, is the disturbance of the gel-sol equilibrium caused by shaking, stirring, ultrasound, or other mechanical factors.] Concussion produces a change in the colloid medium of the cerebral tissue, according to Hallervorden. Boxers may be subject to repeated concussions that, although often subliminal, may be assumed to incur sequelae. This supposition is substantiated by electroencephalographic abnormalities in boxers. It is suggested that, in the absence of focal lesions, the pathogenesis is explained best on the basis of a thixotropic process, leading to premature aging of the brain. These cases emphasize the complexity of the pathological processes and the desirability of careful examination of the brains of former boxers.

PEDIATRICS

Cord-Blood Findings in ABO Haemolytic Disease. G. H. Tovey, E. M. Gillespie, J. Guy and others. Lancet 1:860-863 (April 25) 1959 [London].

The authors studied samples of cord blood collected from 575 babies at Southmead Hospital in Bristol, England, whose mothers were known to be group O, since hemolytic disease caused by ABO incompatibility in the newborn infant is most frequent in babies born of group O mothers. In 393 of the 575 infants the baby's blood group was O, i. e., "compatible"; in the remaining 182 infants it was A or B, i. e., "incompatible." Of the 393 blood group O infants, 23 (6%) were deeply jaundiced, 113 (29%) were slightly jaundiced, and 257 (65%) were not jaundiced. Of the 182 blood group A or B infants, 18 (12%) were deeply jaundiced, 54 (28%) were slightly jaundiced, and 110 (60%) were not jaundiced. The incidence of slight jaundice thus was not significantly different in compatible and incompatible infants. By contrast, deep jaundice was more frequent in the ABO incompatible infants. The hemoglobin level in the cord blood samples obtained from compatible infants was neither in range nor in mean significantly different from the cord blood hemoglobin level of the incompatible babies. While the mean of the serum bilirubin level in the cord blood samples obtained from compatible infants did not differ significantly from that in the incompatible infants, there was a difference in range (0.6 to 3.5 mg. per 100 cc. in the compatible infants, and 0.5 to 4.7 mg. per 100 cc. in the incompatible infants).

Hemoglobin and serum bilirubin levels in the cord blood samples did not correlate well with the clinical progress of the infant, and a cord hemoglobin level below 16.6 Gm. per 100 cc. or a bilirubin level above 3 mg. per 100 cc. is not necessarily an indication for an exchange transfusion in this condition. The modified direct antiglobulin and sodium chloride solution fragility tests, proposed by Rosenfield, and the reticulocyte counts did not facilitate the diagnosis. Deep jaundice appeared earlier and more frequently after ABO heterospecific pregnancy than homospecific pregnancy. The highest over-all incidence of neonatal jaundice was in babies immature by age of gestation, and it was not influenced by ABO incompatibility. The clinical assessment and cord blood examination thus showed the need for caution in the interpretation of cord blood findings in infants thought likely to show ABO hemolytic disease. Exchange transfusion for ABO hemolytic disease is not necessary unless the serum bilirubin rises to dangerous levels. This can be determined only by close observation and repeated measurement of the serum bilirubin level.

Studies on the Occurrence of Bacteremia in Rheumatic Fever. C. J. Marienfeld, G. Scheff, E. Hackett and D. Jones. J. Chron. Dis. 9:334-352 (April) 1959 [St. Louis].

This study which is based on findings obtained from cultures of blood in 185 patients with rheumatic fever, and in a comparable series of 100 nonrheumatic contratest patients, deals with the possibility that an enterococcus-like organism may serve to continue the rheumatic fever instigated by group A streptococci. The ages of the patients ranged from 5 to 15 years. Three hundred eighty-five blood cultures were obtained from the 185 patients with rheumatic fever, and 124 blood cultures were drawn from the untreated 100 patients in the contratest group. Fifty of the 100 patients had afebrile illnesses, and 50 had febrile illnesses of various types.

Of those patients in both groups who had received no treatment, the results on the occurrence of bacteremia were as follows: Diplostreptococcus organisms were found in 66% of the 36 patients with rheumatic fever in the acute stage, in 22% of the 9 patients in the convalescent stage, and in 10% of the 53 patients in the inactive stage. The percentage of positive cultures, including staphylococcic contaminants, was 14% in the febrile contratest patients and 12% in the afebrile contratest patients. The high percentage of positive cultures in the rheumatic patients appeared to be related to both the acuteness of the disease and the absence of antibiotic or salicylate medication. The organisms obtained have been identified as being most closely related to the enterococcus group of streptococci, most of them belonging to group D. It is suggested that the presence of these organisms in the blood stream may be an indication of their importance in the pathogenesis of the rheumatic process initiated by group A beta-hemolytic streptococci.

Vaccination Against Whooping Cough: The Final Report to the Whooping-Cough Immunization Committee of the Medical Research Council and to the Medical Officers of Health for Battersea and Wandsworth, Bradford, Liverpool, and Newcastle. S. Bedson, P. Armitage, W. C. Cockburn and others. Brit. M. J. 1:994-1000 (April 18) 1959 [London].

The authors report the results of field trials with 7 different pertussis vaccines made in various parts of England; in these trials 13,029 children attending local authority clinics were inoculated and followed up for 2 or 3 years. The results of the trials clearly showed that it was possible to produce by vaccination a high degree of protection against whooping cough, as shown by the substantial reduction in the attack rate among home contacts, and, in those cases in which vaccination failed to give complete protection, it was possible to reduce the severity and duration of the disease. The different vaccines employed varied in their protective action. Of 2 vaccines prepared in liquid medium, one was not significantly different in its protective properties from the vaccine prepared on solid medium; the other was significantly different, but the reason for this was not clear and the number of observations was small. The protective antigen extracted from Hemophilus pertussis by Pillemer and co-workers in 1954 was, in the concentration used, more effective in its protective action than a whole bacterial vaccine, but caused more reactions. The protective action induced by a pertussis vaccine mixed with diphtheria toxoid (F. T.) was similar to that induced by the same pertussis vaccine alone.

The results of serologic tests in the trial of the mixed vaccine showed that the diphtheria antitoxin response was slightly less in a group of children receiving 3 doses of the mixed vaccine than in a similar but slightly older group of children who received 2 doses of a purified diphtheria toxoid precipitated by aluminum phosphate (PTAP). Serologic tests were also made of the ability of the pertussis vaccines to produce specific agglutinin in mice and in children. The results, together with those previously obtained, were compared with the degree of protection afforded in children. A general correlation was obtained with whole bacterial vaccines between protection and agglutinin production, but not with Pillemer's antigenic fraction. Thus, agglutinin production cannot always be taken as evidence of protective activity.

The 7 vaccines were assayed for their protective potency by the intracerebral mouse protection test, and their relative potencies were compared, together with those of the 18 vaccines used in previous studies. A comparison between the results of the field trials and the laboratory tests of all 25 vaccines showed a high degree of correlation between the potency of the vaccines in protecting mice against intracerebral infection and their ability to protect children against pertussis. These findings confirm the previous observations and strengthen the conclusion that only those pertussis vaccines which have been shown, by the intracerebral mouse protection test, to have an adequate potency in relation to the British standard pertussis vaccine should be used in prophylaxis against whooping cough.

Complications of Influenza and Its Relationships with Pulmonary Tuberculosis in Children. C. Caione, I. Santillo and V. Gammarrota. Ann. Ist. Carlo Forlanini 18:385-400 (no. 4) 1958 (In Italian) [Rome].

All 52 children, between the ages of 1½ and 13 years, who were being treated for pulmonary tuberculosis on the pediatric ward of the Carlo Forlanini Institute in Rome, contracted influenza during the 1957 epidemic of Asian (type A) influenza. Four of these children also presented bronchiectasis and a polycystic lung. Some children suffered from mild diffused bronchitis with asthma. In 6 children bronchopneumonia developed 2 or 3 days after the influenza and, in general, affected the base of the lungs. This complication was favored by posttubercular bronchiectatic alterations in 3 children and by congenital malformations in 1. The inflammation disappeared within 5 or 6 days, with the exception of one child in whom it lasted longer. Three children had slight or temporary attacks of fever as a result of subacute tonsillitis, and 2 had purulent otitis media. Peripheral circulatory insufficiency was observed in 12 children; during convalescence these children suffered collapse, combined with nausea, perspiration, slow pulse, and arterial hypotension. Examination after recovery from influenza showed slight myocardial involvement in 7 children, but this involvement was no longer present after 2 months.

Some hemorrhage with increased vasal fragility was observed in 10 children. Several children during the first 2 days of the influenza showed neurological involvement. A delayed energizing effect of the illness was noticed in those whose organic resistance diminished and an unfavorable evolution of the tuberculosis followed. Erythrocyte sedimentation tests gave high values in all the children; after 2 months these values had returned to preinfluenza levels in 42 children, had increased in 6, and had improved in 4. All the children lost weight during the illness, but afterward most of them regained some weight; two, however, remained stationary, and one lost more weight. Roentgenologic examinations made 2 or 3 months after the influenza showed that in all but 3 children the course of the tuberculosis had not deteriorated. Tuberculin reaction showed hyperergia in one of these 3 children and diminution of skin reactivity in another.

Short-Term Hormone Therapy: Its Effect in Active Rheumatic Carditis of Varying Duration. M. G. Wilson and Wan Ngo Lim. New England J. Med. 260:802-807 (April 16) 1959 [Boston].

In a previous report of the effect of short-term hormone therapy in 55 patient attacks of active carditis of 3 to 21 days' duration, the authors had demonstrated that in the majority of the patients early adequate hormone therapy for an average period of 7 days resulted in no overt residual cardiac damage. This study is concerned with the effect of short-term steroid therapy in 53 additional patient attacks. The 53 attacks occurred in 47 children, ranging from 3 to 19 years of age, who were observed on the pavilions of the New York Hospital. They received antibiotics during their stay in hospital. The steroids used included hydrocortisone, prednisone, prednisolone, and methylprednisolone. Therapy was given every 6 hours for an average period of 7 days, and was terminated abruptly. Patients were observed for an additional week, with modified bed rest. The amount of steroids given daily was guided by the circulating-eosinophil response each morning, 4 hours after the last medication. Five patients required a second course of 7 days of hormone therapy. The duration of carditis before therapy was 21 days or less in 36 patients, and 4 to 10 days in 30 of these. In 17 patients the duration of carditis before therapy ranged from 22 days to 4 months.

Among the 55 patient attacks of carditis in the earlier study and 36 in the present report, when the duration was less than 3 weeks and in the majority less than 10 days, effective short-term therapy resulted in termination rather than suppression of the clinical signs and symptoms of carditis without overt residual cardiac damage. Patients were ambulatory 2 or 3 weeks from the onset of therapy, and their cardiac status, as noted at the end of therapy, was maintained for a follow-up period of 3 months to 8 years. These observations suggest that long-term hormone therapy is probably not required. Of 17 patients in initial and recurrent attacks of carditis of 22 days' to 4 months' duration, progressive symptoms of carditis were terminated without further increase of residual cardiac damage beyond that present at the onset of therapy.

The gross and histological findings in 38 patients with carditis of variable duration, who received symptomatic therapy between 1934 and 1938, revealed that predominantly reversible lesions characterized the findings among children with carditis of short duration, in contrast to the minimal reversible lesions and extensive irreversible damage sustained when the carditis was of longer duration. In 24 initial attacks of short duration, in which new systolic and diastolic murmurs were present, the valve leaflets were delicate. The heart weight was 1 or 2 times the expected weight when the duration was less than one month, and 3 or 4 times when the duration was longer. There was a close correlation between radioscopic estimate of heart size and the heart weight. In active carditis short-term hormone therapy will terminate the inflammatory process irrespective of its duration. Only with early adequate hormone therapy can residual cardiac damage be expected to be prevented or minimized.

An Inborn Error of Lipid Metabolism. J. A. Bigler, R. F. Mais, R. M. Dowben and D. Yi-Yung Hsia. Pediatrics 23:644-661 (April) 1959 [Springfield, Ill.].

The authors report a new clinical syndrome characterized by hepatomegaly, retardation of physical and mental growth, and disturbance of lipids in the plasma. The abnormalities were present in 2 siblings born of parents who were second cousins. None of the other 6 siblings was affected. The disturbance, characterized by an increase in the concentrations of triglycerides and phospholipids in the plasma, has been described in detail biochemically. The concentrations of cholesterols were not greatly increased, although there was an alteration in the ratio of the concentration of cholesterol esters to that of total cholesterol. By means of paper and agar-gel electrophoresis, the authors found the disturbance to involve primarily an increase in the concentration of alpha$_2$-lipoproteins. Using zone electrophoresis on starch medium, they showed that there was an increase in the concentrations of phospholipids and triglycerides in alpha$_2$-lipoproteins and of triglycerides in alpha$_1$-lipoproteins. Starch electrophoresis revealed the disturbance to be distinct from that of idiopathic hyperlipemia or primary hypercholesteremia. Ultracentrifugal analysis showed an increase in each of the fractions, but this was most marked in the serum lipoprotein fraction with S_f 20-400. This fits well with the concept that this represents primarily a disturbance in the concentrations of triglycerides and phospholipids, and very little change in cholesterols. This is also compatible with an increase in the concentration of alpha$_2$-lipoproteins.

The presence of a similar abnormality of lipids in 2 siblings of a consanguineous mating provides strong suggestive evidence that this defect is hereditary in origin; most probably it is transmitted by a rare autosomal recessive gene. Since the nature of this lipid abnormality is quite different from that of idiopathic hyperlipemia and primary hypercholesteremia, it should be classified as a new third "inborn error of lipid metabolism."

Carotid Artery Occlusion in Childhood. H. Stevens. Pediatrics 23:699-709 (April) 1959 [Springfield, Ill.].

The inclusive term "infantile hemiplegia" usually implies cerebral venous thrombosis. However, cerebral arterial occlusion may cause hemiplegia in childhood and infancy. The author reports 3 children, aged 1, 5½, and 13 years, in whom the internal carotid artery was the site of the occlusion. The initial onset in the 3 children occurred spontaneously without a history of trauma. In 2 patients the symptom was an ipsilateral severe headache; the third patient was unable to move the right arm or leg on awakening in the morning. The clinical manifestations and course were identical with those of carotid artery occlusion in adults. The diagnosis can be made sometimes on the basis of clinical data alone. Diagnosis can be suspected from the history of a "stuttering" pattern of recurrent, stereotyped, focal neurological involvement, appearing hours to months before the hemiplegia appears. Mental symptoms and papilledema are common. A valuable diagnostic sign is a transient or permanent Horner's syndrome ipsilateral to the carotid artery thrombosis. Palpation of the carotid arteries, a useful but too often neglected technique, may provide the decisive sign, justifying the diagnosis and justifying the use of carotid arteriography.

The cause of spontaneous nontraumatic carotid artery occlusion in childhood remains a mystery. Only a few instances have been reported. Disseminated vascular degeneration may involve the carotid artery in some instances, or an isolated atheromatous plaque may be responsible. Elaborate investigations, including multiple laboratory tests, should be made to establish a primary cause for the occlusion, such as an associated endocardial fibroelastosis which was detected in 1 of the 3 children. This child died, while the other 2 recovered completely.

It is suggested that therapy be directed toward preventing complete thrombosis, or the extension of the thrombosis, in a presumably isolated lesion which is probably due to localized arteriosclerosis. This reasoning further warrants conservative medical treatment as against surgical treatment of acute spontaneous carotid artery thrombosis in children. In instances of arterial spasm or other nonthrombotic obstruction, prophylactic use of anticoagulants should be considered, since thrombosis is likely to follow if spasm is sustained.

Lymphopneumatosis Cystoides Intestinalis With Eosinophilia in the Infant. J. Gagnon and M. Rheault. Pediatrics 23:710-717 (April) 1959 [Springfield, Ill.].

Lymphopneumatosis cystoides intestinalis, also known as intestinal emphysema or abdominal gas cysts, is a relatively rare pathological entity in the infant. The diagnosis of this condition is usually made at autopsy or in the course of an operation. However, crepitations are elicited by deep palpation of the abdomen, and tympanism by percussion. A roentgenogram of the abdomen occasionally will show double-contoured intestinal loops and a generalized reticular image of the abdomen. The presence of pneumoperitoneum and of trapped gas helps in clinching the diagnosis. The gas cysts are sometimes visualized by proctoscopic examination. A history of gastrointestinal distress, especially diarrhea, repeated infections, and the clinical picture of general debility are the usual clinical findings in pneumatosis cystoides intestinalis in the child. The complications which appear to be most frequently associated with the disease are intestinal obstruction and pneumoperitoneum.

The authors studied pneumatosis cystoides intestinalis in 5 infants, ranging in age from 15 days to 5 months; autopsies were performed on these patients from 2½ to 18 hours after death. The disease had a duration of from 1 week to 2 months. All the patients presented nonspecific lesions typical of the stage of "exhaustion" of the "adaptation syndrome." The lungs of all 5 patients contained evidence of acute pyogenic inflammation in the form of bronchopneumonia, abscess formation, or diffuse parenchymal infiltration. In all the infants bacteria were found to be present in the intestinal lumen and in some of them in the lamina propria of the mucosa and on the serosa; there were also lesions of enteritis of various intensity. The lamina propria was infiltrated by numerous polymorphonuclear leukocytes, 80% of which were eosinophils. In the submucosa the leukocytes were less numerous, and again they were practically all eosinophils; they appeared to have no immediate topographic relationship to the cysts. Eosinophils could be seen in the sinuses and in a great number at the periphery of the lymph node in 2 patients. In one patient in whom eosinophils were abundantly present in the lymph node, some rhomboid, elongated, acidophilic crystals resembling Charcot-Leyden crystals were found within the reticulum. The authors attempted to elucidate the association between lymphopneumatosis cystoides and eosinophilia and came to the conclusion that the gases in the cysts are not able to produce eosinophilia. Lymphopneumatosis seems to result from the association of several factors, namely, gastrointestinal disturbances and acidification of the gastrointestinal content. However, the pathogenesis of the condition is still obscure.

Galactosemia: Genetic Considerations. R. Van Geffel, A. Devriendt, J.-P. Dustin and others. Arch. franç. pédiat. 16:158-184 (no. 2) 1959 (In French) [Paris].

Four infants afflicted with galactosemia were diagnosed by 2 criteria: (1) appearance of notable galactosuria after ingestion of milk and (2) abnormal increase in galactosemia after ingestion of 1.75 Gm. of galactose per kilogram of weight. These 4 infants were from 3 different families. In the first family the first 3 children died after serious symptoms; as a result, in the last 2 born in this family the diagnosis of galactosemia was suggested very early, based on the cited criteria. In the other 2 families, in spite of early diagnosis, many symptoms developed in a short time. In the 4 infants omission from the diet of foods with galactose was followed by a rapid remission of symptoms, and no sequel was observed. The parents of 3 of the infants had intolerance to galactose, which only an "oversupply" test could show. This indicates the role of heredity in this disease.

The aminoaciduria which accompanies galactosemia is frequently at a high level and may exist several days after the disappearance of galactosuria, when the patient is deprived of all galactose. The authors used methods of partition chromatography to estimate the amount of aminoacidemia and of aminoaciduria. These determinations showed the importance of "overflow" phenomena of the tubular resorption capacity, but some ascertainments permit the belief that there is some measure of intervention of purely renal factors.

A Functional Investigation of Liver Impairment Due to Poliomyelitis. G. Poli, G. Verdura and N. Svilokos. Minerva pediat. 11:215-226 (March 3) 1959 (In Italian) [Turin, Italy].

Laboratory tests were made on 49 poliomyelitic children to study the extent of liver impairment from a functional point of view. The tests indicated liver damage in 6 of 8 children on whom they were made during the acute stage of the disease. A marked drop in the level of gamma globulin was observed in the remaining 2 children; the alpha$_2$ globulin value was high, and the beta globulin not so high; marked hypoalbuminemia and hypoproteinemia were observed in one child. Some relationship between the extent of liver damage and the neurological involvement was found in some of the 8 children.

The tests in the other 41 children of the series were made 3 to 11 months after the acute episode of poliomyelitis. These children were divided into 3 groups according to the results of the tests. The first group, composed of 14 children, showed a normal protein picture, with the exception of a somewhat constant increase in alpha$_2$ globulin. In these children the serum lability tests gave negative results; bilirubinemia was normal or had increased only slightly; total cholesterinemia had reached maximal normal values in 3 children only, and it was slightly lower than normal in 1 child. The few changes present in these 14 children did not indicate a sclerotic effect of the hepatic lesion. The 6 children of the second group presented a normal total protein picture and an increase in globulin values which caused an inversion of the protein quotient. Electrophoresis revealed hypoalbuminemia and increased alpha$_2$, gamma, and, at times, alpha$_1$ globulin; colloidal lability tests were positive in all cases; van den Bergh's test gave results close to normal; bilirubinemia was close to normal; the values of cholesterol were normal in all children except one in whom they had increased. An accurate examination of the clinical history of each of these 6 children made possible the exclusion of poliomyelitis as the cause of these alterations. One child had suffered a lipid nephrosis, and the others had contracted Asian influenza a few days before the tests were made. The third group was composed of 21 children, all with a normal protein picture. Electrophoresis showed an increase in alpha$_2$ and, at times, in beta globulin; the gamma globulin level was low in all these patients. Other tests gave normal results. Gamma globulin values were low in 23 of the 49 children observed.

The authors believe that liver damage observed during an acute episode of poliomyelitis is benign even in extreme cases of hepatitis and that the pathological changes regress with no fear of liver cirrhosis even after a long period of time.

Acute Appendicitis in the Course of Measles: Description of 5 Cases. P. Nicola and L. Bertola. Minerva pediat. 11:237-242 (March 3) 1959 (In Italian) [Turin, Italy].

The authors report on 5 children operated on for acute appendicitis during the course of measles. The children, 5 to 8 years old, were observed at the University Hospital in Turin, Italy, during the period from April to July, 1957. All the children recovered and were discharged from the hospital 8 to 21 days after admission. Statistical data on the frequency with which acute appendicitis occurs during measles are not available, but the authors believe that it would be unwise to assume that such an occurrence is exceptional. The symptoms of appendicitis developed in the prodromal stage of the measles in one child, coincided with the cutaneous eruption in 3 other children, and developed when the exanthem had almost disappeared in the 5th child. The symptoms in 2 children were characterized by a gradual onset, with vague and diffused abdominal pain which later became localized and severe; in the other 3 children the symptoms were severe after their sudden onset. One child presented a hyperemic and edematous appendix free from adhesions, while 4 children presented an appendicular perforation, which was followed by circumscribed peritonitis in 3 cases and general peritonitis in the other. Two children suffered from intestinal occlusion as a late complication. A rapid and severe evolution of acute appendicitis constitutes the most characteristic symptom of the condition during the course of measles.

UROLOGY

Dissolution of Experimentally Induced Vesical Calculi in Rats by Sodium Phytate and Sodium Neutral Phosphate Treatment. D. F. McDonald and M. O. Orallo. J. Urol. 81:534-536 (April) 1959 [Baltimore].

The authors performed experiments on rats in which growth of vesical calculi was induced by implantation of magnesium nidi. The animals then were given high doses of sodium phytate and sodium neutral phosphate mixed in the ground laboratory chow. Both phytate and phosphate administrations were associated with complete dissolution of 50% of the experimentally induced calculi and reduction in size of those calculi not completely dissolved. These animal experiments confirm clinical reports and suggest that optimal dosage is of utmost importance in achieving dissolution of urinary calculi.

Partial Nephrectomy for Hypernephroma in a Solitary Kidney: A Case Report. W. K. Kerr, S. Anthone, R. Anthone and N. C. Carruthers. J. Urol. 81:509-511 (April) 1959 [Baltimore].

The authors report the case of a 46-year-old woman who was admitted to the Toronto General Hospital because of total painless hematuria for 5 days and suprapubic pain for 1 day. Cystoscopy revealed that bloody urine came from the right ureteral orifice and no left ureteral orifice was found. An intravenous pyelogram showed compression of the right upper major calyx with an irregular mass in the upper pole of the right kidney. A right thoracoabdominal incision was made through the 9th rib bed. The right renal mass was visible as a probable hypernephroma of the upper half of the kidney, and this was dissected free, exposing the renal pedicle. The renal artery was clamped and the kidney surrounded by Penrose drains filled with ice water to apply local hypothermia. After 11 minutes of cooling, the cor temperature had not fallen, but the surface temperature had fallen to 30.8 C (87.5 F). The tumor and a cuff of normal renal tissue were removed by sharp dissection. Microscopic examination of the operative specimen revealed a renal carcinoma, extensive areas of which had undergone hyalinization with scattered hemorrhage. Renal hypothermia was largely ineffective due to the large bulk of the tumor. This and the long occlusion time of the renal artery were probably the most important factors in producing acute renal failure postoperatively.

Dialysis was used because of the deteriorating clinical picture and the increasing acidosis. Its effects were dramatic and were followed by continued improvement in the clinical state of the patient. The serum electrolyte values gradually stabilized at normal levels, and the anemia corrected itself spontaneously. A satisfactory immediate result thus was obtained in the treatment of this patient, and continued improvement was observed 4 months after the operation. This is the third case of successful elective surgical treatment of a hypernephroma in a solitary kidney. It is believed to be the first case involving the postoperative use of dialysis.

Urogenital Tuberculosis in the Male: Investigations with Vesiculography and Urethrography: Preliminary Report. H. B. Mygind. Ugesk. laeger 121:448-454 (March 19) 1959 (In Danish) [Copenhagen].

Vesiculography in patients operated on for tuberculous epididymitis shows changes in the seminal vesicles and ductus deferens on the sick side in all cases and in unilateral epididymitis on the well side in about half the cases. On urethrography and rectal exploration changes in the prostate are found in almost all patients with tuberculous epididymitis. Since similar changes are equally often found in patients with renal tuberculosis but without epididymitis, it is seen that the prostate is always affected in urogenital tuberculosis. Renal tuberculosis was demonstrated in up to two-thirds of the patients with tuberculous epididymitis. Follow-up of patients operated on for tuberculous epididymitis will probably reveal active tuberculosis in many cases. Tuberculous infection of the urogenital system is, as a rule, extensive at the time when a tuberculous epididymitis is diagnosed. The course of tuberculosis in the pelvic organs is insidious, with few and vague symptoms. Tuberculous epididymitis is an important part symptom in tuberculous infection in the genital system.

Hemangioma of the Kidney. J. B. Wallach, A. P. Sutton and M. Claman. J. Urol. 81:515-518 (April) 1959 [Baltimore].

The authors report the occurrence of hemangioma of the left kidney in a 31-year-old woman who was admitted to the Bronx Municipal Hospital Center in New York with fever, chills, left flank pain, and hematuria. Intravenous and retrograde pyelograms revealed moderate hydronephrosis and a radiolucency in the left pelvis with the filling defect of the left upper calyx. Left renal exploration was accomplished, and a normal appearing kidney was observed. There were 3 prominent varicosities about the renal pelvis. The upper pole of the kidney was bivalved, revealing a pedunculated lesion on a narrow stalk. Nephrectomy was performed as the procedure of choice. The final pathological diagnosis was pedunculated capillary hemangioma of the kidney, arising from the renal papilla and protruding into the superior calyx. The postoperative course was uneventful.

Eighty-six cases of hemangioma of the kidney were collected from the literature. The lesion was almost always unilateral and was solitary in 77 of the 86 cases. Half of the patients were more than 40 years old, and age was not useful in differentiating hemangioma from carcinoma of the kidney. The diagnosis was rarely made clinically; a clue to the diagnosis may be the finding of hemangioma of the skin, but this is infrequent. Various methods of therapy are summarized, including nephrectomy. When the diagnosis of hemangioma can be established by gross and frozen-section examination of the locally excised lesion, the kidney should be closed, and irradiation therapy instituted. Irradiation therapy of hemangioma of the kidney, instead of nephrectomy, deserves adequate trial for the maximum conservation of renal parenchyma.

PATHOLOGY

Studies on Melanoma: II. Sex and Survival in Human Melanoma. L. P. White. New England J. Med. 260:789-797 (April 16) 1959 [Boston].

The author employs the term "melanoma" to denote a malignant tumor derived from the melanoblast (or melanogenoblast) which is capable of spread and metastasis; elsewhere it has been known as malignant melanoma, melanocarcinoma, or melanosarcoma. An investigation was started concerning possible differences in the growth of melanoma between men and women, when it was learned that melanomas, after transplantation into 2 strains of mice, grew 4 or 5 times as large in males as in females during the same period. Survival in human melanoma was studied in 439 determinate cases from a total number of 871 cases obtained from Stanford Hospital and from the tumor registry of the Department of Public Health of the State of California, which conducts follow-up studies for many of the hospitals in California. These cases were grouped according to the site of the melanoma (ocular or cutaneous) and the sex and age of the patient.

The literature was scanned with attention to reports detailing sex and age in patients with melanoma and reporting 5-year survivals. Some series showed a considerable difference in 5-year survival between men and women, and this difference invariably favored the survival of women. Most reports on melanoma, however, did not differentiate between men and women, so that no impression could be formed of the relative survival rates of the two sexes. All reports mentioning pregnancy indicated that pregnancy was a distinct threat to survival in women with melanoma, but none compared survival of pregnant women with that of nonpregnant women of the same age. Statements regarding the deleterious effect of pregnancy on the course of melanoma were based mostly on case reports and not on adequate statistical study.

Data obtained in the aforementioned 439 cases and from the literature suggested that the distribution of melanoma is roughly equal in the 2 sexes, but that survival is better in women than in men with melanoma, and that this difference in survival is statistically significant. Women with melanoma have a greater chance than men of living for 5 years, and the prognosis for survival beyond the 5-year period even more strikingly favors women. The prognosis for 5-year survival in both sexes decreases with advancing age. Although there is no direct evidence, the variation of behavior of melanoma at times of hormonal upheaval in human beings, together with better survival in women than in men, suggests the possibility that melanoma is under some sort of hormonal influence or control.

Experience with Smears of Aspirates from Bone Marrow in the Diagnosis of Neuroblastoma. P. C. Gaffney, C. F. Hansman and G. H. Fetterman. Am. J. Clin. Path. 31:213-221 (March) 1959 [Baltimore].

The recognition of neuroblastoma cells in bone marrow smears from patients with neuroblastoma and the diagnostic value of this finding have been established. The authors report observations on bone marrow smears from 31 of the 35 patients with neuroblastoma or ganglioneuroblastoma, who were observed at the Children's Hospital of Pittsburgh during the 4-year period from July 1, 1951, through June 30, 1955. The bone marrow aspirates were taken on one or more occasions from one or more sites. The sternum was usually the site when only one sample was taken. The tibia, spinous processes of vertebrae, and iliac crest were other sites of aspiration. In 13 of the 31 patients, only one sample was obtained. In each of the remaining 18 patients, from 2 to 6 specimens were taken, either as part of the original examination or at a subsequent examination. Smears were prepared from the aspirates, but no histological sections were made of the aspirated material, because, in the experience of the authors, the study of the sections adds nothing to the knowledge obtainable from smears. Sternal aspirations in infants and young children require great caution because of the danger of penetration of the needle beyond the sternum with damage to vital structures. In young infants tibial puncture may be a less dangerous procedure.

Characteristic tumor cells were found in 15 of the 31 patients. In 13 of the 15 positive cases, the smears of marrow contained tumor cells when the patients were first observed. In 11 patients, the examination of smears of marrow provided the first morphologic evidence of neuroblastoma. The recognition of neuroblastoma cells in smears of marrow suggests metastatic neuroblastoma. All 15 patients with marrow metastases, as revealed in smears, were dead within one year after diagnosis. The longest survival period was 11 months; the arithmetic average of survival time was 3.6 months. Of the 16 patients with proved neuroblastoma or ganglioneuroblastoma, in whom aspirates from bone marrow were negative, 7 are alive and well at the time of this report.

The presence of tumor cells in the bone marrow of patients with neuroblastoma is not dependent upon the existence of radiovisible bone lesions. The early bony metastases involve marrow spaces and hemopoietic tissue rather than osseous tissues proper. The involvement of marrow in neuroblastoma tends to be diffuse. In every instance in which smears of sternal marrow were positive and further search was made in other bones, one or more additional sites proved to be positive. This was true in 7 of the 15 positive cases. In the other 8 patients, no further search was made.

Investigators who have studied the morphologic characteristics of neuroblastoma cells in bone marrow smears have stressed the tendency of the cells to form ball-like clumps or mosaics. The term "pinwheel mosaic," as applied by some, is strikingly apt. The authors do not suggest that examination of smears of aspirates from marrow should replace other morphologic methods in the diagnosis of neuroblastoma, but in view of the nonspecificity of the presenting signs and symptoms in patients with neuroblastoma, the examination of smears of aspirates from marrow for tumor cells may often provide the solution for an otherwise baffling case.

RADIOLOGY

Roentgenokymographic Investigation in Patients with Patent Ductus Arteriosus Accompanied by, or Free from, Pulmonary Hypertension. C. Quaglia, R. Gentilli, and E. Ciambellotti. Minerva med. 50:233-249 (Jan. 31) 1959 (In Italian) [Turin, Italy].

Roentgenokymographic investigations were carried out on 21 patients with patent ductus arteriosus, who ranged in age from 6 to 35 years; 17 of them, having only slight or no pulmonary hypertension, underwent surgery, whereas the remainder were not operated on because of high pulmonary hypertension and the inversion of the shunt. The investigations began a few days before and were continued for 1 to 12 months after the operation. Postoperative roentgenokymograms recorded remission of the increased pressure of hilar arteries in those instances in which it was present before the operation. The width of the sphygmic wave of the pulmonary artery diminished in all the patients, and the pattern of the pulse curve tended to reflect low or normal blood flow. Decrease of the systolic wave was observed in 2 instances. The convexity of the diastolic part of the curve leveled off in 10 patients and attenuated in the remainder. The diastolic-systolic ratio diminished in all the patients. Roentgenokymograms of 4 patients, in whom patent ductus arteriosus was associated with considerable pulmonary hypertension, revealed the state of a perpetuating pulmonary high blood pressure and gradual diminution of the flow of pulmonary circulation. Short and distant roentgenokymographic inspections after the operation indicated that surgical therapy considerably corrected, although it did not completely remove, the anomaly underlying the pulmonary hypertension in these patients.

The Small Intestine in Whipple's Disease. W. Martel and F. J. Hodges. Am. J. Roentgenol. 81:623-636 (April) 1959 [Springfield, Ill.].

"Intestinal lipodystrophy" was the term suggested by Whipple, and he believed the disorder named after him to be due to abnormal fat metabolism. The disease has a progressive downhill course, with death within a few years. Polyarthritis which may be the initial symptom usually disappears after the onset of diarrhea. In about half of the cases diarrhea or abdominal pain is the presenting symptom. The diarrhea is intermittent; the abdominal pain may be crampy and may be associated with distention. Gross rectal bleeding and generalized purpura may be seen in the later stages of the disease. Emaciation and a peculiar gray-brown pigmentation of the skin are typical. Generalized, discrete, peripheral lymphadenopathy is frequently observed. Anemia is almost always hypochromic or normochromic microcytic. A flat oral glucose tolerance curve is characteristic, and there is usually an abnormal increase in fecal fat.

The authors describe their observations on 3 patients with Whipple's disease, giving particular attention to the roentgenologic changes in the small intestine. Two of the patients were men, aged 35 and 54 years, respectively. Both died, and autopsies were made. In one of these men cecal volvulus developed, which may have been coincidental. The third patient was a 43-year-old woman, in whom the diagnosis was verified by biopsy studies on a mesenteric lymph node, on the omentum, and on the duodenal mucosa. The roentgenologic findings in the 3 cases indicate that one can expect the appearance of the small intestine to be abnormal. Thickening of the mucosal folds was an outstanding feature in all 3 patients and was most marked in the duodenum and jejunum. Segmentation of the barium column into large, separated masses was consistently observed. The moulage sign, the apparent obliteration of the mucosal folds in the jejunum ("as if wax had been poured into it"), was not seen in the 3 patients presented here. It is emphasized that various conditions are capable of producing alterations in the roentgenologic appearance of the small intestine which are indistinguishable from Whipple's disease. It will usually be necessary to rely on the clinical and laboratory data in the differential diagnosis.

The wall and the mesentery of the small intestine are thickened in Whipple's disease. The mesenteric and retroperitoneal lymph nodes are enlarged, yellowish in color, and have a spongy appearance on sectioning. Microscopically, one notes a diffuse infiltration of the mucosa of the small intestine by large mononuclear macrophages which possess abundant granular cytoplasm imparting a foamy appearance to the cell. The cytoplasm stains faintly basophilic with hematoxylin and eosin and gives a positive reaction to periodic acid Schiff (P.A.S.) reagent. These cells are present in the mesenteric and retroperitoneal lymph nodes and have been demonstrated in peripercal lymph nodes as well. The lacteals in the small intestine are dilated and frequently contain these macrophages together with collections of neutral fat and fatty acids. The mucosal villi are swollen due to the cellular infiltration, and the submocosa may be edematous. Little attention was paid to the cytoplasm-rich macrophages until Black-Schaffer in 1949 showed that these cells reacted positively to the P.A.S. test. It is possible that the P.A.S. positive material is elaborated by the intestinal mucosa and phagocytosed by the mononuclear cells, or perhaps it originates within these cells. The abnormal protein-polysaccharide complex may be related to certain enzymes necessary for fat absorption and transport. A beneficial response of Whipple's disease to corticotropin, but not to cortisone, has been reported, and the possibility of a genetic factor in the etiology has also been suggested.

Acromegaly. H. L. Steinbach, R. Feldman and M. B. Goldberg. Radiology 72:535-549 (April) 1959 [Syracuse, N. Y.].

The authors report on 11 men, between the ages of 24 and 53 years, and on 16 women, between the ages of 30 and 73 years, with acromegaly from whom roentgenograms were obtained. Acromegaly, an insidious disease, is the result of increased secretion of growth hormone by a benign or, rarely, a malignant tumor of the anterior pituitary occurring during or after closure of the epiphysial cartilages. Symptoms and signs are due to the expansile growth of the neoplasm, the elaboration of excessive quantities of pituitary hormone, and the interference with other normal pituitary functions by pressure of the tumor on the uninvolved portion of the gland. All the tissues in the body are affected by the excessive quantity of growth hormone. In general, the response is one of hyperplasia and hypertrophy. The bones may increase in size, owing to accelerated endochondral ossification or oppositional bone growth. In some areas there is increased bone resorption. Some of the changes occurring in the bones are similar to those incident to the normal aging process, but are markedly accelerated and greater in degree. The usual sex differences in the appearance of the soft tissues and skeleton are exaggerated by the excessive quantity of growth hormone.

The diagnosis of acromegaly is primarily clinical. The roentgenologic diagnosis could be accurately established in an examination of the skull if the sella turcica were significantly enlarged and if this finding were accompanied by an elongated mandible with a wide angle and enlarged sinuses. The presence of a thick scalp and of hyperostosis of the inner table of the skull in women would further substantiate the diagnosis. However, this combination of morphologic changes was present in only a few of the patients, and in many of them a diagnosis of the disease by roentgenographic methods alone was not possible. Of particular significance in the patients was the presence of a marked thickening of the soft tissues of the fingers, toes, and scalp. This thickness diminished after successful treatment by irradiation or surgical removal of the pituitary gland, but the tissues did not revert to normal size. Another pertinent roentgenologic observation was the association of thickened articular cartilages (wide joint spaces) of the hands and wrists with hypertrophic changes of the adjacent periarticular surfaces. A peculiar constriction of shafts of the proximal phalanges and metatarsal bones of the foot was observed in most of the patients. The results of this study indicate that roentgenograms of the feet should be obtained, along with those of the skull and hands, in the routine evaluation of acromegaly. Concave posterior borders of the lumbar vertebrae were observed in 6 patients. This change could be due to increased molding resorption of the central posterior surfaces of the vertebral bodies as a direct result of the excessive quantity of growth hormone or, secondarily, of pressure by the enlarged soft tissues in the spinal canal.

Familial Pulmonary Alveolar Microlithiasis: Four Cases from Colombia, S. A.: Is Microlithiasis Also an Environmental Disease? G. Esguerra Gómez, E. Lichtemberger, A. Santamaría and others. Radiology 72:550-561 (April) 1959 [Syracuse, N. Y.].

The authors report the occurrence of familial pulmonary alveolar microlithiasis in 4 women, between the ages of 40 and 50 years, who were sisters and belonged to a family of 7 children (2 boys and 5 girls). This disease, which is characterized by the presence of innumerable minute concrements lying free within the alveoli, throughout the lungs, and unattached to the alveolar walls, is an extremely rare disease, and the 4 cases were the first to be discovered in Colombia. The results of roentgenologic and clinical studies, the course of the disease, and the anatomico-pathological findings on autopsy in the oldest of the 4 patients with the most advanced lesions were in accord with those reported by other workers in the 43 cases of familial pulmonary alveolar microlithiasis collected from the literature. In 3 of the 4 sisters, a pleural thickening over the minor interlobar fissure was a constant finding in the roentgenograms of the chest; none of these patients had cough. Cough is not considered a symptom of uncomplicated alveolar microlithiasis, and does not appear so long as cor pulmonale does not supervene. In the 4th patient who had the most advanced lesions and who died, there was, however, cough, either dry or with scanty sputum of the mucous type, and the roentgen-ray picture was that of cor pulmonale.

The electrocardiographic tracings of the 4 patients did not show definite myocardial damage in the ventricular complexes, except for a highly questionable blockage of the bundle of His. The earliest manifestations of the disease were dyspnea and cyanosis, which, however, were not proportionate to the severity of the lesions as revealed by the roentgenograms. In some patients these symptoms appear early, whereas in others they may be almost nonexistent even though the lesions are far advanced. The possibility that microlithiasis may not be exclusively familial but that environmental and dietetic factors may play a role in its onset in persons previously predisposed was suggested by the fact that the 4 patients lived all their lives in the same house and in the same locality, with the same environment and the same diet, while the other siblings who left home at an early age did not show any evidence of the disease. So characteristic is the roentgen-ray appearance that the roentgenologist who has once seen a chest roentgenogram of any of these patients, and who keeps in mind the paucity of symptoms, can make the diagnosis of microlithiasis with certainty, without waiting for histological confirmation.

Possibilities and Limitation of Roentgenographic Examination in Early Diagnosis of Bronchogenic Carcinoma. A. Giobbi, F. Calamari and E. Miradoli. Lotta contro tuberc. 28:1138-1144 (Nov.-Dec.) 1958 (In Italian) [Rome].

A mass roentgenographic examination conducted among 704,837 persons in Milan, Italy, revealed bronchogenic carcinoma in 1.98 persons per 100,000; the frequency among persons over 40 years of age (148,340) was 9.43 per 100,000. The carcinoma could still be treated by surgery in most of these patients. It appeared as an isolated mass in 16 patients and was accompanied by an atelectatic component in 2. The tumor, however, was no longer operable in 6 patients; in one it appeared isolated but with some metastases in the hilar-mediastinal lymph nodes, and in the other 5 it was accompanied by parenchymal atelectatic processes. As limitation of roentgenographic examination in early discovery of carcinoma, the authors list the following conditions: (1) failure of the examiner in recognizing early signs of bronchogenic carcinoma; (2) location of the tumor is such that radical operation is not allowed even in case of early diagnosis; and (3) histological characteristics of the tumor in cases of rapid local growth and rapid metastases. The authors believe that the optimal frequency of roentgenographic examination for constant control of bronchogenic carcinoma in a community is every year or two, but even this frequency may fail to reveal early enough the presence of tumor in some cases.

Myelography with Water-Soluble Contrast Substance: Analysis of 427 Myelograms. P. Kolstad and G. H. Solem. Nord. med. 61:306-309 (Feb. 19) 1959 (In Norwegian) [Stockholm].

Myelography with a water-soluble contrast medium (myelotrast, abrodil) is considered a reliable diagnostic examination for nucleus prolapse and a valuable supplement to clinical examination. An accuracy of 90 to 95% should be attainable. Completely lateral prolapse may escape myelographic demonstration, and other intraspinal conditions, such as arachnoiditis or vascular malformations, can myelographically resemble prolapse. From 1949 to 1957, a total of 427 myelograms were obtained for 393 patients, aged from 16 to 74 years. The diagnosis was incorrect in only 12 of the 173 patients on whom laminectomy was performed. Myelotrast undoubtedly exerts an irritating effect on medulla and nerve roots. A slight fall in blood pressure may be expected, and the injection should be done by an experienced person. The complications observed are not thought to justify departure from the method. The authors look forward to a less irritating, i. e., more isotonic, contrast medium.

Left Atrial Calcification. C. W. Vickers, O. W. Kincaid, F. H. Ellis and A. J. Bruwer. Radiology 72:569-575 (April) 1959 [Syracuse, N. Y.].

The authors report on 3 women, between the ages of 36 and 59 years, and 2 men, aged 44 and 57 years, respectively, in whom calcification in the wall of the left atrium was revealed by chest roentgenograms. All 5 patients had severe rheumatic heart disease with involvement of the mitral valve. Pure stenosis of the mitral valve was present in 4 patients who underwent mitral commissurotomy. The 5th patient had severe mitral insufficiency, and this patient was not operated on. Invariably the history of symptoms referable to rheumatic heart disease was of long standing, the range of its duration being from 7 to 51 years. The cardiac disability was severe in each patient. In addition to calcification in the wall of the left atrium, the roentgenologic findings in each patient indicated severe mitral heart disease with pulmonary venous hypertension. Calcification of the mitral valve of sufficient degree to be identified roentgenologically or surgically was noted in 3 of the 5 patients. The calcification of the left atrial wall was of such magnitude or in such a position in 3 of the 4 patients operated on that the surgeon was compelled to enter the left atrium by some approach other than the usual one through the auricular appendage. The patient, in whom the atrium was entered through the calcified posterolateral wall, died 24 hours postoperatively.

It is believed that entering the atrium through the calcified wall, through the normal atrial wall near the valve, or through a pulmonary vein—the 3 possibilities of approach to the mitral valve in case of calcification of large portions of the wall—may be associated with a greater than average risk. The total number of recorded cases in which the ante mortem diagnosis of calcification of the left atrial wall was established by roentgenologic methods is now 42. Because of the density of the heart shadow and the superimposed shadow of the thoracic spine, the calcification may not be observed in the conventional roentgenogram of the thorax. It may be best revealed by roentgenoscopy, by roentgenograms in the right anterior oblique and lateral projections, or by overpenetrated Bucky films made in the posteroanterior projection. It may be readily revealed by means of tomography.

Intramural Aortic Dissection as a Complication of Translumbar Aortography. E. F. Wolfman and D. E. Boblitt. A. M. A. Arch. Surg. 78:629-638 (April) 1959 [Chicago].

The authors report 4 men, between the ages of 37 and 62 years, with aortic and peripheral vascular disease, on whom translumbar aortography was performed. These patients died, 3 hours, 29 days, 4 days, and 12 days, respectively, after the aortography. Autopsy which was performed on 3 of the 4 patients revealed that 2 died as a direct result of a dissecting aneurysm of the abdominal aorta produced by the injected contrast medium. Although a dissecting aneurysm was proved at autopsy in the third patient, ventricular fibrillation and coronary insufficiency accounted for his death. In the case of the patient in whom permission was not granted for autopsy, it was conceivable that occlusion of the renal arteries occurred, but the presence or absence of dissection could not be substantiated. A more likely explanation for renal failure in this patient was the direct toxic effect of a large concentration of contrast medium acting on the renal parenchyma.

Intramural injection of contrast medium into the aortic wall is a common and potentially fatal complication of translumbar aortography. Of 302 translumbar aortograms obtained at the University Hospital and the Veterans Administration Hospital in Ann Arbor, Mich., between July, 1951, and June, 1958, there were 33 intramural injections, representing an incidence of 10.9%. They included the 4 reported by the authors. The following suggestions are offered for minimizing this complication. A short beveled needle should be employed in performing the aortic puncture. To minimize dissection of the frequently diseased medial layer by the needle tip, the aorta should be pierced as closely as possible to a 90-degree angle. Unless visualization of the upper abdominal aorta or kidneys is required, the needle should be inserted below the second lumbar vertebra. If a view of the upper aorta is necessary or lower aortic obstruction is suspected, the vessel should be pierced above the visceral branches, at the T-11 or T-12 level. No contrast medium should be injected unless a good pulsatile flow of arterial blood issues from the needle hub with each systolic thrust. A test picture should always be obtained after the injection of 5 cc. of contrast medium to detect aberrant locations of the needle tip. The aorta should be punctured only once, and the total amount of contrast medium injected should be limited to 25 cc.; frequently less will suffice. Rapid manual injection should be used, rather than high-pressure mechanical devices. A delayed abdominal roentgenogram should be obtained 20 minutes after the last injection of contrast material to detect abnormal retention of iodides by the kidneys and gastrointestinal tract.

BIOCHEMISTRY

Phospholipids of Human Red Blood Cells. G. B. Phillips and N. S. Roome. Proc. Soc. Exper. Biol. & Med. 100:489-492 (March) 1959 [Utica, N. Y.].

The authors feel that the wide disagreement in values reported for concentrations of individual phospholipids in human red blood cells indicates inadequacy of methods employed. Recently, it was shown that the main phospholipids in serum lipid extracts could be isolated and quantitated by chromatography on silicic acid. Concentrations of individual serum phospholipids in these studies were at variance with many previously reported values. In the present study, the same chromatographic method was used to isolate and quantitate the main phospholipids of red blood cells of 3 male and 3 female apparently healthy young adults in the fasting state. Three extractions of hemolyzed red blood cells were routinely performed, after it was found that the first 3 extractions removed probably more than 95% of the total extractable phospholipid. Chromatography of red blood cell lipid extract on silicic acid revealed the following main components: (1) ethanolamine-containing and serine-containing phospholipid, (2) lecithin, (3) sphingomyelin, and (4) lysolecithin. No previous investigators reported the presence of lysolecithin, which comprised about 2% of total red blood cell phospholipids. It is unlikely that this represented adsorbed serum lysolecithin, as the red blood cells were washed 3 times, or that it was produced as an artifact during the extraction or isolation procedure. It is of interest to note the striking contrast in the relative proportions of individual phospholipids in red blood cells as compared with serum, especially since there is evidence for exchange of phospholipids between these 2 compartments.

The values found for relative concentrations of individual serum phospholipids with the method described here were at variance with results obtained by others. Previous reports revealed considerable variation between normal subjects in the same series, as well as between series of different investigators, suggesting inadequacies in methods employed. The method described in this report resulted in relatively good agreement between duplicate samples and rather slight variation between subjects. Moreover, the present method seemed relatively simpler than previous methods and was carried out on only 2-ml. aliquots of packed red blood cells, although a considerably smaller quantity could have been used. At least as much lipid phosphorus appeared to be extracted as with previous methods.

Comparative Study of the Effect of Corn Germ Oil and Butter in Experimental Dyslipidosis in the Rat. C. Briot, J. Carlotti, P. Laudat and others. Presse méd. 67:543-545 (March 21) 1959 (In French) [Paris].

Experimental dyslipidosis was produced in 140 male Wistar rats by the administration of 14 diets differing chiefly in the character of their lipid overloading with either butter or corn germ oil. Each diet was given to a group of 10 rats for from 21 to 30 days, after which the animals were killed and their lipid status determined. Comparison of the findings in the groups that received 2 diets identical in general composition but differing in the type of lipid calories supplied, i. e., butter in one diet and corn germ oil in the other, revealed an absolute parallelism in the lipid formulas and a close parallelism in the lipoprotein reactions. Some doubt, therefore, in regard to the possible effect of unsaturated fatty acids on the lipid-protein balance seems to be warranted. It may be, as some works tend to show, that the provision of large quantities of unsaturated fatty acids, while permitting the persistence of lipid-protein imbalance, especially hypercholesterolemia, is nevertheless unfavorable to the deposition of lipids in the walls of the arteries. This point of view, however, is entirely foreign to that expressed by the American authors of the original work on this problem.

The literature reflects the differences of opinion between authors who have studied the action of unsaturated fatty acids in man and those whose studies, constantly less favorable, have been carried out in the rat. One reason for these differences may perhaps be found in the small number of patients who have actually been studied well, so that the favorable results might be attributable to a fortunate chance. The chief criticism that can be addressed to human experiments, however, is a lack of distrust in regard to possible psychological factors: thus, the use of a placebo seems to diminish considerably the part supposedly played by the introduction of unsaturated fatty acids into the diet.

The results of the present animal experiments, on the other hand, do not necessarily or even probably hold good for man. The causes of the dyslipidosis sometimes found in patients with atherosclerosis are, in fact, not known, and certainly it is never associated with alimentary errors as gross as those imposed in this study. The signs of atherosclerosis in a given patient may be the anatomic sequelae of an earlier humoral disease of which it is useless to try to find any biochemical traces. Nevertheless, humoral changes must necessarily be relied on, at least in human experiments on atherosclerosis, but in studying them care should be taken to use a large enough series and to counteract psychological influences by the rational administration of placebos.

Effects of Dietary Fat Upon Polyunsaturated Fatty Acids of Blood in Patients with Multiple Sclerosis. B. Gerstl, W. E. Davis Jr., J. K. Smith and others. Proc. Soc. Exper. Biol. & Med. 100:534-538 (March) 1959 [Utica, N. Y.].

Two schools of thought on the etiology of multiple sclerosis have recently gained prominence; one suggests that an allergic reaction is involved, the other that an enzymatic or metabolic defect underlies recurrent attacks of demyelination. The authors feel that their own observation that some patients with multiple sclerosis revealed higher plasma levels of dienoic acid than did controls, together with the dietary studies of Swank and the increased chylomicron index noted by Skillen and others, warrants further investigation of the lipid metabolism in this disease. A baseline blood sample was obtained after a patient with multiple sclerosis had been on average hospital diet, including approximately 20% protein, 28% fat, and 52% carbohydrate. Then, the test patients and contratest patients all received a nearly eucaloric diet with soybean oil as main source of polyunsaturated fatty acids (PUFA). Blood was obtained after overnight fasting. Clotting of blood was prevented by addition of dry potassium oxalate. The cells were separated by centrifuging at 3,000 rpm. Plasma was extracted and total lipids and cholesterol determined as in previous investigations. The PUFA's were measured by the method of Herb and Riemenschneider. Measurement at 374 mμ was included, and the PUFA's were calculated according to Hammond and Lundberg. Separation and estimation of PUFA's in red blood cells were carried out as described elsewhere.

Since ratios of individual lipids to total lipids and those between the 2 groups of structurally related PUFA's are more revealing than data on individual lipids, the authors also report their results as ratios. The different ratios obtained are listed, and some of the data obtained are compared with those of other investigators. The concluding summary emphasizes that a decline of cholesterol/lipid and of tetraene/PUFA and an increase of PUFA/lipid as well as diene/PUFA ratios were observed in both groups of patients. Differences between the 2 groups are represented by significant decline of triene/PUFA ratio in the contratest group and, conversely, by a rise of triene/tetraene ratio in the patients with multiple sclerosis. Studies on the red blood cell lipids did not reveal any significant changes in the ratios, though they reflected to a slight degree the changes in plasma lipids.

MSH-like Substance from Human Placenta. H. H. Varon. Proc. Soc. Exper. Biol. & Med. 100:609-610 (March) 1959 [Utica, N. Y.].

A melanocyte-stimulating hormone (MSH) from the pituitary, which is of functional importance in lower animals, has been known for several years. Interest in this hormone was renewed in 1954 after Lerner and co-workers showed that MSH had a role in human physiology. These investigators also reported that blood and urine levels of this hormone were elevated during pregnancy. The author of this paper describes studies that aimed at isolating MSH from human placenta. The isolation procedure employed is a modification of that employed by Lerner and others for preparation of pituitary MSH. Full-term placentas, of an average weight of 550 Gm., were collected from Chicago Lying-in Hospital soon after delivery, and then extracted individually.

The final product of extraction averaged 120 mg. per placenta. The assay employed was similar to the in vitro frog skin method. However, the skin of Anolis carolinensis (chameleon) was substituted because of certain advantages. Selected lots of hog pituitary MSH were used as standards. The material extracted was a tan powder readily soluble in water. The activity decreased greatly within a matter of weeks during storage at room temperature. Loss of activity was slowed down by refrigeration. The substance caused darkening of Anolis carolinensis skin similar to that caused by hog pituitary MSH. A table lists results of assays of MSH preparations from 10 placentas. The average concentration was about 3.05×10^2 units per milligram. This activity is much less than the reported value for pure MSH from hog pituitary of 5×10^7 units per milligram. The material had a potency 1/200 to 1/300 of that found in MSH preparations from hog pituitary.

The material seems to be present in concentrations greater than can be accounted for by its being derived from placental blood. Conjecture regarding the biological significance of placental MSH is summarized as follows: The rapid decline of MSH values in blood and in urine soon after delivery might be due to loss of the placenta containing large quantities of this substance. Whether the formation and rapid postpartum loss of much of the increased dermal and mucosal pigmentation commonly noted during pregnancy (chloasma) is also related to placental MSH requires further study.

Effect of Spirolactone SC 8109 on Renal Function in Normal Human Subjects. R. A. Wiggins, M. E. Hutchin, J. V. Carbone and P. D. Doolan. Proc. Soc. Exper. Biol. & Med. 100:625-627 (March) 1959 [Utica, N. Y.].

A natruretic effect of synthetic steroids (spirolactones) has been demonstrated in rats, dogs, and human subjects, but it has also been shown that these spirolactones are virtually ineffective in the absence of mineralocorticoid and that effects upon urinary electrolyte excretion are constant so long as a constant ratio of spirolactone/mineralocorticoid is maintained. It was the purpose of this study to examine more carefully renal function in the normal human subject under the influence of endogenous aldosterone with and without administration of a spirolactone. The substance used was 3-(3-oxo-17beta-hydroxy-19-nor-4-androsten-17alpha-yl)propionic acid gammalactone known by the code name, SC 8109. Five normal, male, human subjects were studied by the classic clearance techniques during salt deprivation before and after therapy with the steroid-17-spirolactone, SC 8109. No change in the glomerular filtration rate or effective renal plasma flow could be demonstrated, but a definite sodium diuresis and potassium retention occurred in response to the spirolactone. A small increase in free water clearance was seen in 4 of 5 subjects studied. These observations localize the effect of spirolactone to the renal tubule.

PUBLIC HEALTH

Lung Cancer and Cigarette Smoking. R. Doll. Acta Unio internat. contra cancrum 15:417-423 (no. 2) 1959 (In English) [Louvain, Belgium].

The author reports the results of 2 studies on lung cancer and cigarette smoking and reviews the various hypotheses which have been suggested to account for the results. Data on 187,783 men, between 50 and 69 years of age, who died of lung cancer in the United States have been compared with data on 24,354 men, aged 35 years or over, who died of the same disease in Great Britain. The first group was followed up for nearly 4 years, and the second for more than 6 years. The mortality rates among all the men, including nonsmokers and smokers, were about 10 times greater than the rates among nonsmokers, and the mortality rates among heavy cigarette smokers were about 20 to 30 times greater than those among nonsmokers. The mortality rates among cigarette smokers were substantially greater than the rates among other types of smokers, and the mortality rates among mixed smokers of cigarettes and other types of tobacco were intermediate. The mortality rate was lower when smoking had been stopped for 1 to 10 years, and was substantially lower when smoking had been stopped for 10 years or more.

The author concludes that the association of lung cancer and cigarette smoking is not an artifact resulting from the method of study. It does not necessarily follow that smoking causes the disease. It is suggested (1) that smoking determines the site of cancer appearance, (2) that the precancerous condition induces smoking, and (3) that smoking and cancer result from a common factor (heredity, alcohol). The principal observations which have been cited as incompatible with the theory that cigarette smoking is a causal factor in the production of the disease are (1) the increasing disparity in smoking habits, (2) the disproportion between the mortality from lung cancer and the cigarette consumption in different countries, and (3) the conflict of evidence with regard to the apparent effect of inhaling. These 3 objections raise questions of considerable theoretical interest. Many more data are required before they can be answered completely. It seems reasonable to conclude that none of the data provide a compelling reason for abandoning the hypothesis of causality.

Epidemiologic, Experimental and Histological Studies on Metal Cancers of the Lung. W. C. Hueper. Acta Unio internat. contra cancrum 15:424-436 (no. 2) 1959 (In English) [Louvain, Belgium].

The author presents data from the literature concerning environmental and occupational exposure to carcinogenic metals, their carcinogenic potency, and their relation to the causation of cancer of the lung. These data indicate that respiratory contact with these metals plays probably a more important role in the determination of general and occupational incidence rates of lung cancers than has been assumed in the past by many investigators. Recent studies on the distribution of certain metals in the atmosphere of some American cities suggest that lung cancer hazards for residents of industrialized urban areas not only may be due to organic chemicals but may, perhaps in part, be related to the presence of carcinogenic metallic dusts. The marked differences in the concentrations of various metals in the atmosphere of the numerous cities analyzed, moreover, suggest that these differences may have contributed to the striking variations in lung cancer death rates noted recently in a survey of 163 American metropolitan areas. This observation does not support the allegation that local differences in smoking habits mostly account for the differences in lung cancer death rates.

The author reports on his own experimental investigations with radioactive metals, chromium, and nickel, which have succeeded in the production of cancers of the lung and of other tissues in animals exposed to certain inorganic chemicals (radioactive metals, nickel, chromium, arsenic, asbestos, and, possibly, iron oxide and beryllium); these are known to be or are suspected of being responsible for an excessive occurrence of cancers of the lung, larynx, nasal cavity, and nasal sinuses in members of special worker groups. The histological, hyperplastic, and neoplastic lesions elicited in the lungs of experimental animals by nickel-containing and chromium-containing compounds were similar or identical with those seen in men exposed to the same and similar inorganic carcinogenic dusts, fumes, and vapors. The cancerous reactions observed in animals and man include carcinomas of the squamous-cell, round-cell, and adenocarcinomatous types. Animals exposed to nickel and chromium exhibit, moreover, sarcomatous reactions. Since there is abundant human and experimental evidence indicating that the same exogenous carcinogen is capable of producing cancers of different histological types, the recently advanced claim that squamous-cell and round-cell carcinomas of the human lung are predominantly, or almost exclusively, caused by cigarette smoking has no sound scientific or factual basis.

Salmonellosis Traced to Sea Gulls in Ketchikan Area. A. N. Wilson and Mrs. R. Baade. Alaska Med. 1:18-19 (March) 1959 [Anchorage].

It has been observed that, with the onset of the storms of early winter, the sea gulls leave the water front of Ketchikan and fly inland to Ketchikan Lake for shelter. Epidemics of gastrointestinal disease, generally referred to as "stomach flu," are often observed at this time of the year. In November and December, 1953, such an outbreak was traced to sea gulls at Ketchikan Lake, which is the main source of the water supply of the town. Thousands of gulls were at the lake at that time, and the water showed gross contamination. Birds are known to be carriers of Salmonella organisms. Of 14 sea gulls collected for study, one was found to harbor Salmonella (paratyphoid) organisms. Stool specimens obtained from hospitalized patients during the epidemic were also found to contain these bacteria. Typing of the organisms isolated from the gull and from the patients proved that all were of the type Salmonella manhattan, an organism of the paratyphoid C group. The authors cite additional reports on the pollution of water supplies by sea gulls, including instances in Massachussetts and at various points along the Pacific coast in Canada and the United States.

BOOK REVIEWS

The Practical Evaluation of Surgical Heart Disease: The Grover Clinic. Written and compiled by Robert G. Trout, M.D. Edited by Robert P. Glover, M.D. Medical illustrator: Joseph Sunner. Heart sounds recorded by J. Scott Butterworth, M.D. [Adapted from American Medical Association convention exhibit (June, 1957) which was awarded Billings Gold Medal.] Cloth. $10. Pp. 132, with illustrations and one 45 r. p. m. recording. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1959.

This manual was prepared primarily as an uncomplicated and ready reference work to help the busy physician in his everyday professional tasks. The following subjects are presented: simplified physiology, radiographic interpretation, electrocardiographic interpretation, patent ductus arteriosus, coarctation of the aorta, vascular rings, pulmonary stenosis, interatrial septal defects, interventricular septal defects, tetralogy of Fallot, transposition of the great vessels, mitral stenosis, mitral insufficiency, aortic stenosis, aortic insufficiency, coronary insufficiency, cardiac catheterization, angiocardiography, and a bibliography. Each subject receives about five pages in the book and contains a drawing of the lesion, a discussion in outline form, roentgenograms, electrocardiograms, and a comment on the history, examination, and treatment of one or more illustrative cases. The presentation of each subject is brief and easily understood. This manual contains a wealth of information based on the extensive experience of the authors. If a practitioner were desirous of having a surgeon discuss one of these subjects, this is about what the latter would say in a brief discussion, accompanied by illustrations. This book is a primer on these subjects, and as such it is valuable.

No reference is made to such other cardiac conditions that concern the surgeon as acute and chronic compression of the heart, penetrating and nonpenetrating wounds of the heart, tumors of the heart, foreign bodies in the heart, the physiology of localized versus generalized anoxia in the heart, self-electrocution of the heart, and reversal of the death factor after it appears. These subjects also concern the practitioner but they are not common, except electrocution in hearts that are structurally too good to die. Prevention of electrical death and reversal after it occurs should be included in a modern treatise on cardiac surgery. This manual, however, covers a lot of ground in a concise and understandable way, and it is highly recommended.

Enzymopathologie: Enzyme in Klinik und Forschung. Von Dr. med. Roland Richterich. Cloth. 128 marks. Pp. 703, with 132 illustrations. Springer-Verlag, Heidelberger Platz 3, (1) Berlin-Wilmersdorf (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1958.

The author has been a student of enzymology, first in the departments of anatomy and of internal medicine at the University of Basel and, more recently, in the United States in the departments of cancer research, internal medicine, and pharmacology of the Boston University School of Medicine. He is co-author of publications dealing with hyaluronidase, urease, the effect of benzidine on liver, phosphatase, hydrogenase, and others. Thus he is well qualified to discuss authoritatively a subject which has become increasingly important for the understanding of human physiology and pathology. In the course of the extremely rapid growth of the knowledge in this area, it has become difficult to keep up with the literature even of one's own country, to say nothing of publications in other countries. The purpose of this book is to supply a critical digest of what is known of the role of enzymes in pathogenesis of disease, at least, as of the date of writing.

The subject is treated in three parts. Part 1 deals with the biology and physiology of enzymes. In part 2, general aspects of enzymopathology are presented. Inheritance of enzyme systems, the role of enzymes in the metabolism of proteins, carbohydrates, lipids, porphyrin, hemoglobin, and nucleic acid, in nutritional disturbances, and in hormone metabolism are among subjects discussed in detail. The role of enzymes in cancer, in the various aspects of proteolysis, and in the reactions of the body against external damaging agents are some of the other topics. Special enzymatic pathology is treated in over 300 pages of part 3. The role of enzymes in the lesions of connective tissue, of the osseous system, muscles, cardiovascular system, stomach, pancreas, liver, kidneys, and male sex organs are covered in great detail. The name and subject indexes are well organized.

The author has done a good job of assembling much of the material in the bibliography and presenting it in the form of a coherent text. In the field of causative relation between enzymes and human pathology there are not many textbooks of this type, and contributions of this sort are bound to be useful. However, this book, like others of the same kind, suffers from an inevitable weakness that cannot be avoided in ambitious projects undertaken by a single author. Some parts are more extensively treated than others. An example of a field that

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

could be improved by bringing the background knowledge up to date is the discussion on anaphylaxis and proteolysis in the sixth chapter of the second part of the book (page 248). The observations made in the last 10 years by H. Tabor, R. W. Shayer, S. A. Karjala, and others with respect to the metabolism of histamine have not been included. The most "recent" references on the subject of histamine date back to 1951.

Despite this and other similar shortcomings, ideas are clearly presented throughout the text, and this makes the book highly commendable not only for the specialist, and the professional investigator, but even more so for the interested physician who tries to acquire a better understanding of the biochemistry of human disease.

Leprosy in Theory and Practice. Edited by R. G. Cochrane, M.D., Ch.B., F.R.C.P. With foreword by Sir George McRobert, C.I.E., M.D., F.R.C.P. Cloth. $15. Pp. 407, with 190 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; John Wright & Sons, Ltd., 42-44 Triangle West, Bristol 8, England, 1959.

This new, comprehensive textbook on leprosy and its management was compiled from the contribution of 24 students and practitioners in the field. The editor and major contributor is a dedicated and hard-working scholar whose travels have kept him in close touch with colleagues in those areas of the world where leprosy is endemic. He writes easily with authority and from long familiarity with his subject.

The chapters are in the familiar sequence of a text that deals with a communicable disease, exploring in order the history, bacteriology, epidemiology, pathology, immunology, clinical course, complications, treatment, prognosis, and prevention of the disease. The pace of the text changes as chapters by the contributing authors introduce detailed accounts of special problems and their management. The chapters on the acid-fast bacteria and on other mycobacterial diseases provide studies of the footings upon which further knowledge of the causative organism of leprosy will undoubtedly be built. The work on epidemiology shows the puzzles and contradictions that experience with leprosy provides to the field worker. It is difficult to derive sets of principles from observations gathered, and the sound conclusion is that "statements which apply in one area may not apply in another area."

An interesting chapter on sensory and neurohistological changes in leprosy follows the chapter on the pathology of the disease. There are very thorough presentations on involvement of the eyes, the care of the feet, and physical therapy methods for the relief of deformity. The excellent chapter on the surgical management of deformity, particularly of the hand, is well illustrated and should be useful to orthopedic surgeons concerned with restoring the function of hands crippled by other diseases of the peripheral nerves. There are 10 appendixes on topics that present problems to clinicians, surgeons, laboratory workers, and public health administrators. There is a surprisingly small number of repetitions or of contradictions in a book composed of chapters by authors whose laboratories and clinics are physically separated from each other by oceans.

There is a theme in the foreword, the chapters, and appendixes that reiterates many times the need for an objective examination and an understanding of this enigmatic disease, without emotional bias. It is expressed in many ways with sympathy for the plight of the patient. For example, the chapter on deformity begins by recognizing that visible mutilation frequently associated with the disease has maintained an unreasonable public rejection of these patients. Another chapter shows sensitivity to the hope that can now be encouraged in patients with leprosy and the misery and fear that still haunt them.

The editor and the contributors are all practical men faced with the need to combat a great clinical and public health problem. The only criticism that one can make of this useful book is that it devotes too little space to speculation and to theory. Each contributor adapts theory to his needs so that it becomes "practice." One gets the sense from this book that leprosy as a topic of study can serve as a springboard into the study of medicine and that the many unsolved problems in this disease will eventually be mastered by a multidisciplinary approach.

Instrumentation in Anesthesiology. By William H. L. Dornette, M.D., Professor of Anesthesiology and Head of Department, University of Tennessee College of Medicine, Memphis, and Verne L. Brechner, M.D., Assistant Professor of Anesthesiology, University of California School of Medicine, Los Angeles. Cloth. $8. Pp. 242, with 130 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1959.

Medical instrumentation is a field of constantly increasing ingenuity, particularly since World War II. At least one American graduate school now offers opportunities for advanced studies in this imaginative and eminently useful branch of invention. A volume that includes descriptions of all the devices and instruments currently applicable to anesthesiology has long been needed. This book satisfies that need. The authors proceed from such fundamental but salient considerations as safety precautions, basic physics, and electrical interference to the highest developments which instrumentation has thus far reached, meaning servomechanisms and central monitoring systems.

This presentation of a diverse and complex subject is unusually well done. The illustrations in many cases help to reduce what otherwise would have been a lengthy description. The reader who wishes additional information, particularly from authorities in the field who did pioneer work in the development of a given instrument or procedure, is provided with references to such studies. The authors lay down six fundamental requisites which, they believe, must be satisfied if a monitoring device or, indeed, any instrument applicable to anesthesiology, is to be acceptable. These are efficient performance, practical size, simplicity of operation, equitable cost, minimal nuisance to patients and others, and maximal safety. The book has great potential usefulness, since every technique and procedure it describes should contribute in some measure to improvement in the care of the surgical patient.

Asexualization: A Follow-up Study of 244 Cases. By Johan Bremer, Medical Director, Gaustad Mental Hospital, Oslo, Norway. Cloth. $5.50. Pp. 366. The Macmillan Company, 60 Fifth Ave., New York 11; *Oslo University Press*, Oslo, Norway, 1959.

From time to time through the years someone comes up with the suggestion that sexual criminals, or persons who might become such because of uncontrollable sexual urges, ought to be castrated. It is not always clear whether the suggestion has in mind the protection of the public or the penalizing of the individual, but the suggestion is made nevertheless. The practice of castrating criminals has never become popular in the United States and, in fact, in no state is it a legal procedure. It is legal in a number of European countries, however, and this book reports on a series of 244 sex offenders who were castrated under the Norwegian law between 1935 and 1949. The study analyzes in detail the changes in physical and psychic states, emotional reactions, and sexual life brought about in the 216 men and 28 women who were castrated under this law. Psychiatrists especially will be interested in the individual case histories.

So far as castration may be the answer to the problem of the sexual criminal, the conclusions of the report are quite definite. The study of the male castrates concludes: "In general, castration is only of therapeutic significance in behavioral disturbances involving an urge for sexual relief. No general effect of pacification has been encountered at all, no sedative influence on exaggerated affections, no harmonization of emotional life, no 'resocializing' influence on asocial or antisocial behaviour beyond the sexual sphere." About women castrates the report concludes: "Nobody castrated in the hope of pacifying has become easier to handle, and clinging and petting oligophrenics continue to do so. . . . As far as it is possible to judge from such unreliable, psychopathological material, sexual reactivity and activity are not essentially changed . . . . The results of the legal castration of women seem so uncertain and poor that there is definitely doubt as to its justification."

This book should be of great value and interest to lawyers, penologists, and psychiatrists.

The School Health Program: A Textbook for Teachers and for Other Professional Personnel in School Health. By Alma Nemir, M.D., Professor and Director, Division of Health Education, Department of Health, Physical Education, and Recreation, College of Medicine, University of Utah, Salt Lake City. Cloth. $6. Pp. 428, with 70 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Written by a physician, with assistance from numerous educators, dentists, and public health personnel, this volume gives a good over-all view of a typical school health program.

The amount of attention given to the details of the health service program is greater than is customary in books describing the general school health program. Part 1, "The School Child: His Normal Health Status and Common Health Problems," discusses 16 areas of health interest from the point of view of both health service and health education, with emphasis on the role of the teacher, administrator, nurse, doctor, and others on the school health team. Part 2, "The School Health Program," covers the administrative organization of the school health program, including environment, services, education, and evaluation.

Each chapter is followed by a bibliography of additional sources of information and a list of materials for teachers to use in schools. The appendixes include a list of resource agencies, examples of school health record forms, and methods of program evaluation. Repeated reference is made to publications of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association, as well as to other committees and commissions of these and other recognized authorities. The book's universal application is limited, however, by being strictly concerned with the specific school health situation created by the statutes and traditional practice in Utah. Nevertheless, school health personnel who follow this book should be able to develop a reasonably good program.

Physiology of Muscular Activity. By Peter V. Karpovich, M.D., M.P.E., Research Professor of Physiology, Springfield College, Springfield, Mass. Originally by Edward C. Schneider, M.P.E., Ph.D., D.Sc. Fifth edition. Cloth. $5.50. Pp. 368, with 83 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

The present edition is a revised and expanded version of a book recognized for a quarter of a century as an authoritative compilation of useful research in the physiology of exercise. A new chapter on muscle training has been created by dividing a former chapter. New material has been added on the effect of warming up on athletic performance, the heart and training, the relation between physical fitness and intelligence, a comparison of isotonic and isometric methods of muscle training, and other related factors. To serve as a guide to those using this book for study, each chapter is followed by a list of questions suitable for classroom discussion or self-evaluation.

A bibliography of 524 references, each keyed by number to the place of its discussion in the text, makes this a source book for physicians and physiologists concerned with sports medicine, physical educators and coaches responsible for the training of persons engaging in physical activity and athletic programs, and for those involved in research in physical activity.

Dangerous Marine Animals. By Bruce W. Halstead, M.D., Director, World Life Research Institute. Cloth. $4. Pp. 146, with 87 illustrations. Cornell Maritime Press. Cambridge, Md., 1959.

This book was written after 14 years of medical research on marine organisms. Dangerous animals are those that bite or are poisonous to man. This is a practical and instructive guide to their identification, world-wide geographical distribution, habits, noxious effects, and the treatment and prevention thereof. The opening chapter is a brief résumé of the manner in which knowledge of dangerous marine organisms has evolved. Following chapters deal with marine animals that bite (sharks, moray eels, and giant clams); those that sting (jellyfish, cone shells, and stingrays); and those that are poisonous to eat. This last chapter is not concerned with illness due to bacterial food poisoning, but rather with marine animals whose flesh may contain toxic substances under certain conditions. Physicians should be particularly interested in the sections on medical aspects which describe types of wounds, symptoms of poisoning, and recommended treatment. The practical value of this book is increased by numerous photographs and detailed drawings that show the specimen in its natural habitat and illustrate various features of anatomic significance. It is unusual to find authoritative and comprehensive data of this type presented in a popular style. Physicians, first-aid workers, biologists, and skin divers alike should find this a useful and valuable handbook.

The Plasma Proteins: Clinical Significance. By Paul G. Weil, B.A., M.D.C.M., M.Sc., Director, Transfusion Service and Assistant Physician, Royal Victoria Hospital, Montreal. Material published in American Practitioner & Digest of Treatment, September, 1958. Cloth. $3.50. Pp. 133, with 2 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1959.

Plasma proteins play a dominant role in the pathogenesis of a variety of diseases and clinical syndromes. The names of some proteins have become the names of diseases, e. g., agammaglobulinemia, cryoglobulinemia, and macromolecular syndrome. Consequently, at least slight familiarity with plasma proteins is essential nowadays for the understanding of many diseases and for the diagnosis and intelligent therapy of some. The busy physician, be he generalist or specialist, can rarely afford the time to look for information regarding biochemistry in the many textbooks on the subject. This pocket-sized book attempts to bridge the gap between what the practitioner needs and the sources of the required information in books and special journals. The specific items discussed in this book include albumin, fibrinogen, globulins, liver disease, pregnancy, infancy and old age, hemorrhagic disorders, amyloidosis, and other topics. The treatment of these complex subjects is aimed at the person without specialized education in chemistry. The author has achieved what he set out to do. The book is excellent for a quick review of an important subject and for occasional consultation, which will be facilitated by the well-organized subject index.

Tuberculosis Medical Research: National Tuberculosis Association 1904-1955. By VargVinia Cameron and Esmond R. Long, M.D. Historical series no. 9. Cloth. $5. Pp. 325. National Tuberculosis Association, 1790 Broadway, New York 19, 1959.

This is a historical résumé of the research in tuberculosis first recorded by leading proponents from their own laboratories and reported largely at the annual meetings of the National Tuberculosis Association commencing in 1904. The realization of the importance of such research in the solution of the problem of controlling tuberculosis, and that the necessary funds came primarily from the sale of Christmas seals, stimulated the leaders of the abovementioned organization in 1921 to create a definite program of grants-in-aid. Later this program was extended to the medical division, the American Trudeau Society. Thus there came into being one of the first research programs on a national scale supported by public contribution, the forerunner to the many national research programs now operating. This treatise contains a section on the financial aspects of grants-in-aid. Those interested in chest diseases, particularly tuberculosis, will wish to study this important phase of the work of the National Tuberculosis Association.

Principles of Peripheral Vascular Surgery. By S. Thomas Glasser, M.D., C.M., F.A.C.S., Associate Clinical Professor of Surgery, New York Medical College, New York. Cloth. $12.50. Pp. 410, with 32 illustrations. F. A. Davis Company, 1914-16 Cherry St., Philadelphia 3, 1959.

The unprecedented development of vascular surgery has brought forth a number of new monographs on this subject. Among these, Glasser's new contribution is characterized by its clarity of style and by its comprehensive bibliography. There are few illustrations, hardly any of them original. The extensive material lacks organization and some subjects are given undue emphasis. The total impression is that of a broad literary survey, uncritically presented. The general practitioner or the general surgeon performing some vascular operations will not get a balanced picture of the field from this book. For those actively engaged in this specialty, it is a useful source of reference.

QUESTIONS AND ANSWERS

TYPHOID CARRIERS

To the Editor:—*It is generally accepted that typhoid immunizations reduce the incidence and severity of clinical typhoid by producing a significant level of antibody. Clinical cases of typhoid therefore are fewer and milder among vaccinated persons. Does it follow that immunizations will reduce the incidence of typhoid carriers? Is an active case of typhoid necessary for development of the carrier state, or are persons likely to become carriers after having had subclinical infections?*

Hugh W. Randel, M.D., New York.

Answer.—Although typhoid vaccine has been extensively used for many years, direct epidemiologic evidence for its effectiveness in man has been, until recently, meager and of uncertain reliability. A recent, carefully controlled field study in Yugoslavia indicates that heat-killed phenolized vaccine offers substantial but incomplete protection against clinical typhoid fever. There is practically no information on whether vaccination will prevent development of the carrier state. A substantial number of chronic fecal or urinary carriers, when discovered through bacteriological surveys or through search for sources of infection in outbreaks or isolated cases in families, give no history of a recognized attack of typhoid fever in the past. There generally is no information whether they became carriers as a result of an undiagnosed clinical attack or of subclinical infection. It seems probable that vaccination will reduce the incidence of typhoid carriers, at least to the extent that it reduces incidence of the disease, but this opinion is not based on direct evidence.

SPONDYLOLISTHESIS

To the Editor:—*Please recommend treatment for an athletic young man, aged 18, who has a neural arch defect of the fifth lumbar vertebra with first-degree slipping on the sacrum. What are the findings regarding success of operation in such cases?* *G. K. Mahl, M.D., Ironton, Ohio.*

Answer.—Treatment of spondylolisthesis depends somewhat on its symptoms. If the patient described is having pain, probably surgical relief is advisable. If there are no symptoms and the defect was discovered incidentally, operation can be delayed until symptoms develop. There are two basic methods for surgical treatment of spondylolisthesis. One is to graft the bones posteriorly, immobilizing the loose segment between the stable segments above and below. In this patient, this would mean fusion of the fifth lumbar vertebra to the fourth and to the sacrum. Results with this method of treatment usually are good. There are published surveys of patients who have had this operation for spondylolisthesis. In rare instances, anterior fusion of the vertebral centrums is done.

The second type of operative procedure involves decompression of the nerve roots as they pass by the site of the opening in the pars interarticularis. According to more recent concepts of spondylolisthesis, this opening is a result of a fracture that has occurred in the pars interarticularis, with nonunion. Callus, cartilage, and other fibrous elements that form about the fracture encroach on the nerve root. Gill's operation consists of removing the loose neural arch posteriorly and thoroughly decompressing the nerve roots at the site of the pseudarthrosis in the pars interarticularis. This procedure has the added advantage of preventing the loose posterior segment from impinging on the cauda, as it might if it were caught and squeezed between the posterior elements of the fourth lumbar and first sacral vertebrae, especially on hyperextension. Results of the Gill operation are not yet fully known. There have been reports of incomplete relief of back pain. There should be no hesitancy, however, in recommending the traditional spinal fusion for this syndrome of spondylolisthesis in an 18-year-old boy with symptoms.

X-RAYS OF EXPECTANT MOTHERS

To the Editor:—*Many expectant mothers ask if a chest x-ray is injurious to the unborn baby. In the past, it has been considered wise to obtain routine chest x-rays of pregnant women. Is there any evidence indicating they are injurious to the fetus? Is the procedure considered worthwhile?*

Oliver E. H. Larson, M.D., Zumbrota, Minn.

Answer.—There is no evidence that very small doses of ionizing radiation, such as those associated with properly controlled chest roentgenography of the expectant mother, are injurious to a fetus. Moreover, many chest lesions occur in pregnant women which demand prompt diagnosis and treatment in the interests of both the mother and the unborn child. Since such lesions are frequently asymptomatic or produce symptoms easily attributable to the pregnancy, they are detected early only by

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

chest roentgenography. Therefore, it would appear worthwhile to obtain chest roentgenograms in pregnant women. It is preferable to defer such roentgenography until the second trimester of pregnancy, and it is the obligation of the radiologist to take every precaution to minimize the exposure associated with the study by proper selection of roentgenographic factors and materials and by proper filtration and diaphragm of the x-ray beam. To answer patients' questions concerning possible hazards of medical use of x-rays, the following facts may be helpful: First, excessive ionizing radiation may induce undesirable changes of two kinds in an organism: somatic changes in the person receiving radiation and genetic changes in the germ plasm of the person which may ultimately increase the number of undesirable mutations in the population. Second, while the tissues of the fetus are relatively more sensitive to the effect of radiation than adult tissues, particularly in the early weeks of fetal life, there is nevertheless a threshold dose of absorbed ionizing radiation below which somatic effects do not appear to occur. Properly controlled diagnostic x-ray studies of any type rarely, if ever, approach this threshold. Evidence based on studies in other species, however, indicates that there is no threshold for genetic effect. Third, any ionizing radiation absorbed by the germ plasm of the fetus or the mother is, therefore, theoretically undesirable in terms of the future population and should be minimized if possible. Of the many sources of ionizing radiation to which everyone is exposed (such as cosmic rays), the medical use of x-rays is the most readily controlled. Diagnostic x-ray exposure of human beings should be kept to the minimum consistent with good medical management. Thus, the proper use of diagnostic roentgenography becomes a matter of good medical judgment. Unnecessary radiation exposure should certainly be avoided, but, where there is any reasonable expectation that the patient may benefit from a roentgenographic study, it should not be deferred because of unfounded or exaggerated fears.

CARE OF AMPUTATION BELOW THE KNEE

To the Editor:—*Please give advice concerning care and hardening of the stump after an amputation below the knee and prior to fitting of prosthesis. The patient had this amputation approximately six weeks ago, and it is felt that physiotherapy should be started as soon as possible.*

Benjamin T. Strehlow, M.D., Bremerton, Wash.

Answer.—The question implies that there has been no therapy for the amputation during the six weeks after operation, and there is no description of the present condition of the amputation stump. The usual postoperative routine for amputation below the knee begins with active flexion and extension exercises as soon as decrease in pain permits, usually on the third or fourth day. The most important therapeutic principles are to maintain a free range of motion with powerful extension and to insure symmetrical shrinkage during the healing period. After primary healing and removal of the stitches, exercise in the whirlpool, with or without gentle massage to prevent adherent scarring, is often advisable. The contemporary opinion is against any specific measure directed toward hardening of a stump. Treatment is directed toward progressive strengthening of all functioning muscles and the prevention of adherent scars and adherent neuromas that may complicate use of the stump in a prosthesis. Between periods of active treatment, the stump should be properly bandaged with recurrent turns of an elastic bandage that does not cause constricting bands. With primary healing and no complications, most patients with such amputations are ready for measurement and fitting in six to eight weeks after the amputation. If therapy is to be started at six weeks after operation, it should include several periods of active resistance exercises each day with whirlpool and gentle massage under supervision, at least once daily. The stump should be carefully wrapped for proper shaping at all times when the patient is not receiving active treatment.

SCARLET FEVER DIAGNOSIS

To the Editor:—*A marked increase in incidence of scarlet fever has been reported in this area. Other than by clinical impression and throat culture, which only indicates a streptococcic infection, no definite means of confirming or disproving the diagnosis has been found. The "Shultz Carlton" reaction was formerly used, but no drug companies are making antitoxin or antiserums. Is there any other diagnostic aid? Recently, the Dick test has been done in persons with suspected cases early in the course of the disease and 10 to 14 days later. All tests have given positive results. In scarlet fever, should not findings on this test become negative during or shortly after convalescence? Would early effective doses of penicillin prevent progress of the disease and and thus interfere with development of immunity? How soon after the onset of scarlet fever does the result of the Dick test become negative?*

Harold J. Sargent, M.D., Newfoundland, N. J.

Answer.—At present, clinical scarlet fever is an extremely mild disease. During the past 20 years, there has been a sharp decline in both frequency and virulence of streptococcic infections. Now there is a rising incidence, but the disease is seldom severe. Satisfactory diagnosis is not always a simple matter. Although the Dicks maintained that a specific erythrogenic streptococcus is responsible for scarlet fever, Griffith in England reported 30 types of streptococci capable of producing the disease. For a number of years the New York State Health Department has not recognized scarlet fever as a separate entity but calls for the reporting of streptococcic infections "including scarlet fever." When scarlet fever thrived the result of the Dick test was usually negative 10 days or two weeks after onset of the disease, but this did not signify that the nose and throat were free of streptococci. A person with a negative response is not immune to streptococcic infection that may be acquired by contact with a patient with scarlet fever. Under such circumstances, a streptococcic sore throat may develop but there is no eruption on the body surface. A streptococcic infection does not confer lasting immunity. Erysipelas is an outstanding example. Although second attacks of clinical scarlet fever are rare, repetitions of streptococcic sore throats are not uncommon. Penicillin is of value in suppressing and eliminating streptococci. There is no method that will establish active immunity to streptococcic infections.

HEARING IMPAIRMENT

To the Editor:—*A 23-year-old woman with a congenital deviation of the nasal septum and a negative family history was affected by influenza at the age of 13. The onset was characterized by fever, dizziness, and earache on the right. During convalescence, she noticed bradyacusia on the right side. Four years later, examination revealed a 25% reduction in hearing on that side. Medical treatment was carried out intermittently, and neither symptoms nor further diminutions of hearing were experienced. The bradyacusia was attributed by three specialists to three different pathogeneses: otosclerosis, deviated nasal septum, and acute influenzal otitis. Could otosclerosis begin at the age of 13, have an acute onset, and be unilateral? Could it cause mild and nonprogressive bradyacusia for 10 years? What is the prognosis for hearing in early otosclerosis, a congenital deviation of the nasal septum, and an acute middle-ear otitis? Which genetic pattern does otosclerosis follow?*

Joseph Giardina, M.D., Brooklyn, N. Y.

Answer.—The history in this case is not adequate to permit a diagnosis. The question whether loss of hearing in the right ear is due to a lesion of the sound conduction apparatus or to the sense organ and/or nerve can be answered by routine hearing tests. This and other information is needed before an opinion can be given. Otosclerosis may begin at age 13. It may be unilateral but is bilateral in the great majority of patients. The onset may appear to be acute, the patient suddenly becoming aware of hearing loss during the course of acute infection, but acute onset is not characteristic. The disease usually progresses with more or less irregularity. Congenital deviation of the nasal septum is not known to have any influence on otosclerosis. Acute middle-ear inflammation may have an influence on otosclerosis, but reliable evidence is not available. The genetic pattern which otosclerosis may follow is not clear, because it is known that otosclerosis may be present without producing hearing impairment.

FETAL HEART SOUNDS

To the Editor:—*A stillborn fetus, weighing 9 lb. 14 oz. (4,479 Gm.), was recently delivered. It was thought that fetal heart sounds had been heard all through labor. Four experienced observers located what they felt sure were easily audible fetal heart sounds 2 in. to the right of the umbilicus. The placental bruit was in the left flank. On delivery, the fetus showed maceration over the anterior surface of the abdomen. How does one account for the fetal heart sounds? The mother, a registered nurse, said she felt life until she went into labor.* *M.D., New York.*

Answer.—For the obstetrician to be absolutely certain of the presence of fetal heart tones and the patient of fetal activity is at times most difficult. The finding of maceration of the fetus at the time of delivery would definitely prove intrauterine death and rule out the possible presence of fetal heart tones during labor. The only explanation is that there were apparently errors in interpretation of the presence of fetal heart tones and fetal activity.

ACHING AND TWITCHING IN LEGS

To the Editor:—*A patient, 64 years old, has complained for about a year and a half of aching and twitching sensations in both lower extremities, predominantly in the calves and ankles. It has been severe enough to keep him awake at night unless he is under heavy sedation with barbiturates. Normal dorsalis pedis, posterior tibial and femoral pulses are felt. There are short saphenous varicosities bilaterally, with venous stasis changes. When first seen, he had large eruptive stasis ulcers on both lower extremities. Tolazoline, 25 mg. four times a day, controlled these adequately but in no way reduced the disturbing sensation. He has since been given phenylbutazone, various corticosteroids, quinine, diphenhydramine, nicotinic acid, vitamin B_{12} injections, and, finally, Ace bandages, all with no relief. What further studies are indicated, and what additional therapy might be given?*

Leonard A. Winski, M.D., Millville, Pa.

Answer.—It is assumed that this patient's symptoms are unrelated to exercise or may even be improved on his moving about. Hence, they are not due to deficient arterial circulation, at least of the extremities. Nor would the postphlebitic syndrome, as manifested by short saphenous incompetence and stasis ulcer, be responsible for twitching of the calf muscles at night. The blood calcium level might be ascertained. A systematic neurological examination, directed toward motor, sensory, and reflex changes and including spinal puncture, should be considered. A roentgenographic study of the lumbosacral part of the spine might detect congenital or acquired structural deformities or calcification of lumbar arteries feeding the spinal cord. Any protective muscle spasms of the back and radiating pain on motions of the trunk should be noted. Only if all organic causes can be excluded should a functional origin of the symptoms be considered. Such a condition may be present for many years without progression. In fact, reassurance helps more than drug therapy. Self-medication must be discouraged.

DIAGNOSIS OF LEPROSY

To the Editor:—*A woman, aged 32, apparently has leprosy involving the left peroneal nerve. The patient has already experienced spontaneous amputations of all toes on that foot and has complete anesthesia of the anterior portion of the foot. No indurated nerve branches can be felt. The patient gives a history of having had this trouble since she was 5 years of age. How much leprosy is there in the Midwest? What is the best form of treatment? What epidemiological factors must be considered? What is the best way of making an accurate laboratory diagnosis?*

S. W. Scorse, M.D., Joplin, Mo.

Answer.—During the period 1921 through 1958, the following number of patients were admitted to the Public Health Service Hospital at Carville, La., from the Midwest: Illinois, 35; Minnesota, 9; Iowa, 3; Missouri, 11; Kansas, 5; Ohio, 13; Wisconsin, 4; Indiana, 10; and Nebraska, 2.

Missouri's 11 cases were distributed as follows: Essex, one patient admitted in 1925; Independence, one admitted in 1927; Kansas City, two admitted in 1926; St. Louis, six admitted in 1922, 1927, 1932, and 1940; and Winfield, one admitted in 1950. Sulfones, in the form of sulfoxone sodium, glucosulfone sodium, or diaminodiphenylsulfone, are the best treatment available today. Residential history gives more factual suggestive evidence than family history. The disease is endemic in Texas, Louisiana, Florida, and California. Residence abroad in China, Japan, South America, Mexico, or Africa would be of considerable significance. All household contacts and relatives who have had close and prolonged contact with the patient suspected of having the disease should be examined for nerve or skin lesions. Skin smears stained by Ziehl-Neelsen method should be examined for acid-fast bacilli. Biopsy from the affected area should be sent to the U. S. Public Health Service Hospital at Carville and/or the Armed Forces Institute of Pathology, Washington 25, D. C., for examination by competent pathologists who are familiar with the histopathology of leprosy.

SKIN CANCER SUSCEPTIBILITY

To the Editor:—*A light-complexioned man, aged 29, has had numerous keratoses on the face and arms, with several proved to be cancerous. It is necessary for him to work out of doors. He has been instructed to wear a broad-brimmed hat. What kind of ointment or protective lotions might be prescribed? Is there available any sun-screening ointment that contains antimalarial drugs?*

M.D., Alabama.

Answer.—The ingredients of sun screens are chosen for their ability to absorb ultraviolet energy with wave lengths ranging particularly from 2,540 to 2,970 A., for these are the rays most concerned with the production of erythema. Yellow petrolatum used alone has significant sun-screening value. No lotion is likely to protect so well as a thick ointment. The usual ingredients of sun-screening preparations are homomenthol salicylate, menthol anthranilate, digalloyl trioleate, and various derivatives of para-aminobenzoic acid. Incorporation of zinc oxide, titanium dioxide, or bentonite will increase the opacity of the ointment. The fishing guides of the Texas Gulf Coast often use zinc oxide paste and dust talc over it generously. Unexpected blistering reactions occasionally follow contact with para-aminobenzoic acid derivatives, presumably representing cross-sensitivity. Photosensitization by contact occurs occasionally from digalloyl trioleate. Ointments containing homomenthol salicylate or anthranilate with added zinc oxide or titanium dioxide may be recommended. These are available commercially. Sun-screening preparations with antimalarial drugs seem to have received no mention in the literature, but experiments with them should be easy to design. There is no reason to expect them to be superior. That this patient has to work out of doors is open to argument. Aggravation by sunlight of cancer in the susceptible skin of some persons should be avoided at any cost.

TEACHING DEAF CHILDREN

To the Editor:—*Is there a program or textbook of directions which would be helpful to parents of a 3-year-old girl who is apparently completely deaf? She does not talk but seems mentally capable otherwise. It is hoped to teach the parents to help the child phonate sounds and develop as much voice for talking as possible.*

M.D., Montana.

Answer.—There is much fine material available for the parents of deaf children. A particularly good booklet is the one entitled "If You Have a

Deaf Child," a collection of helpful hints and useful information for parents of pre-school-aged deaf children, published for the Illinois Annual School for Mothers of Deaf Children by the University of Illinois Press, Urbana. Information about the Annual School may be obtained from the Division of Special Education, Office of the State Superintendent of Public Instruction, Springfield, Ill. The "Correspondence Course for Parents of Little Deaf Children," developed by Mrs. Spencer Tracy and obtainable from the John Tracy Clinic, 806 W. Adams Blvd., Los Angeles 7, has won widespread acceptance and is particularly valuable in helping parents stimulate the deaf child to speak. A number of pamphlets may be obtained from the Alexander Graham Bell Association for the Deaf, Volta Bureau, 1537 35th St. N. W., Washington 7, D. C. This organization has a parent section which represents 23 parent groups and more than 800 sets of parents throughout the United States who find that working together on their common problems brings many benefits.

PAINFUL PURPURIC DERMATITIS

To the Editor:—*A 24-year-old woman, with no previous serious illness, three months ago developed a painful purpuric dermatitis limited to left lower part of the abdomen and left gluteal area. Since then, she has had recurrent episodes on the left side of the face, left arm, and dorsum of the left hand. Skin biopsy showed no pathology in epidermis and a perivascular infiltrate. Chest x-ray, platelet count, and blood cell count are normal, as is the urine. There is no joint or abdominal pain. What might be the cause, and what treatment should be given?*

M.D., Georgia.

Answer.—The information in the query is inadequate to permit a diagnosis. It would be desirable to know the character of the perivascular infiltrate. Was Perls' test done to ascertain whether hemosiderin was present? What were the results of the Rumpel-Leede test? What was the coagulation time, bleeding time, prothrombin time, and albumin-globulin ratio? Had the patient taken any drugs that could have produced purpura? Thrombocytopenic purpura can be ruled out because of the normal platelet count. There are various nonspecific factors which might conceivably lead to unilateral distribution of purpura, including a preceding contact dermatitis or pressure or trauma limited to one side of the body. A nonthrombocytopenic form of purpura with unilateral distribution would be most unusual. Pain in purpura is also most unusual. The question arises as to whether this patient really had purpura or has some other condition such as a vascular nevus with segmental distribution.

PERSISTENT SCALP FOLLICULITIS

To the Editor:—*A man, aged 35, has had intractable furunculosis of the scalp for 10 years. The patient relates this to earlier furunculosis of the buttocks which improved after a few years. He has received a variety of antibiotics and all the x-ray therapy to the scalp that is considered advisable. Careful attention has been given to cleanliness, and he scrubs with hexachlorophene daily. Please give advice on this problem.*

Benjamin T. Strehlow, M.D., Bremerton, Wash.

Answer.—From the description, it sounds as though this patient is suffering from perifolliculitis capitis abscedens et suffodiens, also called dissecting cellulitis of the scalp. This condition is notoriously resistant to therapy. X-radiation is successful at times, but the dosage must be adequate to produce a temporary epilation. Surgical approaches include wide marsupialization with or without grafting. While this procedure produces scars, the condition is basically a scarring one itself. Incision and drainage of abscesses aid in their resolution. Of conservative measures, corticosteroid therapy offers greatest hope. Triamcinolone, 4 mg. four times a day by mouth, could be given and the dosage increased or decreased as indicated by therapeutic results. However, long continuation of this therapy must be anticipated. Use of broad-spectrum antibiotics, given concurrently with the corticosteroids, is theoretically desirable. Vaccines (such as stock staphylococcus toxoid) are indicated. Locally, wet dressings (especially Alibour water) and antiseptic ointments (5% ammoniated mercury) and/or antibiotic ointments may be helpful. Probably this condition is related, at least therapeutically, to hidradenitis suppurativa of the axillae, groins, and buttocks.

USE OF DEPILATORIES

To the Editor:—*It is recognized that considerable risk is attached to the indiscriminate use of depilatories. Please give information in regard to the product Pellex and to any possible deleterious effects which might follow its use.*

D.A. MacGregor, M.D., Wheeling, W. Va.

Answer.—Products of this type ordinarily contain calcium thioglycollate as their active chemical. This is the same chemical found in cold-waving preparations. In these cosmetics, the concentration of the thioglycollate and the pH of the solution are regulated so that the hair is softened to facilitate giving it a new configuration. In chemical depilatories, these properties are regulated so that the hair will be destroyed. In view of the similarity between the chemical composition of the hair and skin, a preparation that is effective in destroying hair may be irritating to the skin. There is apparently no reason to suspect that this chemical is absorbed through the skin. Any unfavorable reactions which occur will be local and most often take the form of skin irritation. If the product is used, it is advisable that the caution statement on the package be observed carefully. Also, the test area to which it is first applied should be not the face but rather the arm or leg. If no unusual irritation occurs, it is wise to apply the depilatory to a small area of the face initially. If this is satisfactory, then it may be applied to a larger surface. If at any time with repeated use a skin reaction occurs, future use is contraindicated.

SPLENIC ARTERY ANEURYSM

To the Editor:—*A patient, aged 37, has a splenic artery aneurysm, diagnosed by x-ray evidence of calcification in the left upper abdominal quadrant. The surgical literature recommends splenectomy for splenic artery aneurysm, but the radiologist says this condition is quite common in older people and he feels that ignoring it would impose no risk. He considers splenectomy to be an unnecessarily radical procedure in this case. How frequently is accidental diagnosis made of splenic artery aneurysm? Should this condition be ignored?* *M.D., California.*

Answer.—Calcification associated with splenic arterial aneurysm is seen fairly frequently in gastrointestinal x-ray series. Most roentgenologists regard it as being relatively benign. In older persons, it is not considered to warrant splenectomy unless there are symptoms or evidence from repeated studies of aneurysm enlargement. Many are observed over a period of years without change. Recently there has been increased interest on the part of surgeons in performing splenectomy for this condition. More careful studies of the future course of patients who do not have a splenectomy compared with those who do are essential before a definitive answer can be given regarding the indications for operation. In such figures, the mortality from the operative procedure must be included. To the knowledge of this consultant, valid figures of controlled series clarifying this point are not yet available.

COLD WAVE LOTIONS

To the Editor:—*Are there any known or proved allergic reactions to cold wave lotions used by beauticians directly or indirectly for permanent waving? Might certain effects appear after a number of years?* *M.D., Pennsylvania.*

Answer.—When cold wave solutions were first introduced on the market, there was some indication that they might be potential health hazards. However, subsequent investigations indicated that they are safe to use if directions are followed carefully. They are generally considered to have a low index of sensitivity. A significant study was carried out by the Food and Drug Administration over a period of two years on 10 widely used cold wave solutions (Draize and others, Percutaneous Toxicity of Thioglycollates, *Proceedings of the Scientific Section, Toilet Goods Association,* May 16, 1947, page 29). Their conclusions were as follows:

"The majority of complaints of both patrons and operators are probably due to misuse of the products or failure to heed proper directions and precautions. Except in the case of sensitive individuals, the judicious use of these solutions should prove a relatively innocuous procedure.

"In the case of the operators who may be exposed daily to varying amounts of the waving solution, it is believed that protection for their hands is essential."

SODIUM IN INSTANT COFFEE

To the Editor:—*Do instant coffees have a high sodium content? Is it high enough to warrant elimination from low-sodium diets?*

F. L. Troost, M.D., Holt, Mich.

Answer.—According to the National Food and Nutrition Board of the National Research Council, instant coffees have an average sodium content of about 84 mg. per 100 Gm. of the dry product. A cup of coffee made from such products would contain about 4 mg. of sodium. It would therefore be the opinion of this consultant that instant coffee could be incorporated in a low-sodium diet.

PROFUSE SWEATS IN PATIENT WITH DIABETES

To the Editor:—*A 66-year-old diabetic is having attacks of profuse sweating at intervals of between two to five days. They last several hours. He had coronary thrombosis in 1955, from which he made a good recovery, and has moderately advanced arteriosclerosis. The blood sugar level averages 160 to 200 mg.%. When the blood sugar level goes below 160 mg.%, the attacks are just as severe and frequent. When insulin dosage is increased, attacks seem to become worse. The patient has moderate hypertension (180/80 mm. Hg), is 5 ft. 5 in. (165.1 cm.) tall, and weighs 130 lb. (59 kg.). The attacks make him feel weak. Fever is not observed. He is receiving 10 units of regular insulin twice a day and is on a 1,500-calorie diet.*

Franklin L. Wilbur, M.D., Asbury Park, N. J.

Answer.—It is quite possible that this patient's attacks of sweating are due to hypoglycemia. Evidence that would either support or exclude this possibility could be obtained by determining the blood sugar level three or four hours after the injection of insulin or, better still, during an attack of sweating. It is unusual for patients of this age to require two doses of regular insulin daily. A trial with 10 or 15 units of one of the intermediate-acting insulins (NPH or lente) given as a single morning injection would be worthwhile.

SPONTANEOUS ACETONURIA

To the Editor:—*A normally active, well-developed, well-nourished 3-year-old boy on occasions has had a fruity breath. Examination of the urine for acetone with the standard powder has shown a strong positive reaction on these occasions. Evaluation of sugar in the urine has always given negative results. The child has never been manifestly ill. The family history is negative for diabetes. What additional studies are indicated in this child? What is the most likely cause of these findings?* *M.D., New York.*

Answer.—The most likely diagnosis in this patient is starvation. Either the child does not take any food for some hours or he vomits, with resulting acetonuria. This would not be abnormal for a young child, for acetonuria appears easily in childhood. The child might have abnormality of glycogen metabolism, with appearance of acetone because glycogen is not available. But this is relatively rare, and, inasmuch as this boy is said to be well, it may be assumed that this is a feeding problem. Spontaneous acetonuria has been reported from Europe, but not much of it is seen in America. Such spontaneous acetonuria is said to occur only in childhood and gradually disappears without treatment as the child gets older. It does not appear to be a serious manifestation.

LIPSTICK CHEILITIS

To the Editor:—*A patient has tried many different types of commercially available lipstick, all of which produce marked blistering and allergic reaction. What ingredients would cause this reaction? Are there any lipsticks this patient could use?* *F. C. Buffington, M.D., Norman, Okla.*

Answer.—Cheilitis caused by lipstick is not uncommon. The staining dyes used in many lipsticks—eosin dyes or halogen derivatives of fluorescein—are believed to be rather frequent photosensitizers. There are available lipsticks which do not contain eosin dyes, but these are nonindelible and their lasting powers are minimal. They must be requested specifically, inasmuch as most manufacturers of hypoallergenic cosmetics also sell an indelible lipstick with a low concentration of eosin.

Other ingredients ordinarily found in lipsticks are relatively innocuous. They contain a blend of oils, fats, waxes, and perfumes. The fats used may be cocoa butter, hydrogenated vegetable oils, lard, cetyl alcohol, or others. The oils are castor oil, peanut oil, soy bean oil, or other vegetable oils. The waxes used are beeswax, carnauba wax, or spermaceti, as well as mineral waxes, ceresin, and ozokerite. Dyes and lakes are added to the lipstick to provide color. These must come from lots approved by the Food and Drug Administration.

PREDNISONE IN ULCERATIVE COLITIS

To the Editor:—*A man, aged 25, has responded satisfactorily to prednisone, 15 mg. daily, for ulcerative colitis. He has been taking this dosage for approximately three years. During this period he has improved psychologically to the point where he has succeeded in working full time and has made a happy marriage. Is it desirable to reduce the dosage gradually with a view to withdrawing prednisone therapy entirely? What is the present opinion regarding the period of withdrawal? What is the justification for continuing the present therapy without attempting withdrawal?* *M.D., New York.*

Answer.—Three years of continued steroid therapy for ulcerative colitis would seem to be an unusually long time. To discuss future therapy satisfactorily, it would be necessary to know the nature of the patient's colitis, the severity of his illness, the extent of intestinal involvement, and the nature and amount of disability produced. However, it can be said unequivocally that the prednisone dosage should be gradually reduced with a view to discontinuing this therapy entirely. Since he has taken the drug for such a long time, it is suggested the withdrawal period cover at least six or eight weeks.

TEST FOR PHENYLPYRUVIC ACID

To the Editor:—*What is the easiest way to test for phenylpyruvic oligophrenia?* *M.D., Florida.*

Answer.—Phenylpyruvic oligophrenia is a hereditary form of mental abnormality characterized by the excretion of phenylpyruvic acid in the urine and associated with a severe degree of mental retardation. Frequently muscular rigidity, tremor, and ataxia are present. Convulsions may also occur. The chemical defect of such patients is inability to oxidize adequate amounts of phenylalanine into tyrosine. This in turn leads to production of increased amounts of other metabolic end-products. One of these is phenylpyruvic acid, which usually appears in the urine if the level of phenylalanine in the blood serum exceeds 20 mg.%. This substance is usually detected in acidified urine by adding a few drops of a 5% solution of ferric chloride. A characteristic dark green color appears with a minute or two and then, after a time, disappears. Recently, Baird (*J. Pediat.* 52:715, 1958) reported a quicker and, in his opinion, more reliable test. A paper stick is impregnated with ferric chloride and glacial acetic acid and allowed to dry. A positive reaction is said to have occurred if the chemically treated portion of the stick turns green, gray, or dark blue within 60 seconds of its immersion in the urine.

INTERNAL TREATMENT OF WARTS

To the Editor:—*During discussion with a local druggist of a news magazine announcement about a pill to remove warts, he mentioned a proprietary preparation of methionine in tablet form for internal use against warts. Please give information on this. Would such treatment help remove the mild, painless skin growths so common on the faces of aged persons?*

Mary B. Sanford, M.D., Methuen, Mass.

Answer.—This consultant has not been able to find any information on internal treatment for warts, nor has the announcement mentioned been seen. It has been stated (Merck Manual of Diagnosis and Therapy, edited by Lyght and others, ed. 9, Rahway, N. J., Merck & Co., Inc., 1956 p. 1605) that systemic treatment of warts "probably is of little or no value apart from its problematic psychologic effect." The well-known essential amino acid, methionine, is marketed in various forms. Its use as an adjunct in the treatment of liver disease is mentioned in "New and Nonofficial Drugs" (Philadelphia, J. B. Lippincott Company, 1959, p. 636), but no record is found of its promotion as an internal treatment for warts.

WHAT'S IT GOING TO BE, DOCTOR?

To the Editor:—*After a woman bears two, three, or four consecutive children of the same sex, what are her chances of bearing a child of the opposite sex in her next pregnancy? What factors other than chance are operating?*

Arthur J. Barnett, M.D., Monahans, Texas.

Answer.—At each pregnancy there is a 50% chance of producing a child of either sex regardless of the previous children's sexes. After four children of the same sex, the chance is still equal that a child of the opposite sex will be born the next time. The situation is the same as in tossing a penny; there may often be a run of heads, but the chance is still 50% of getting tails at the next toss. National statistics show a slightly greater number of boys born, but this can be ignored for all practical purposes.

IRIDOLOGY

To the Editor:—*Please give information on iridology. The practice consists of diagnosing various body ailments by visual inspection of the iris.*

J. D. Losey, M.D., College Place, Wash.

Answer.—This procedure is of European origin and has been accepted by chiropractors, naturopaths, and similar cultists for a good many years. The story goes that a Hungarian had a pet owl, and that as he was looking into the eyes of the owl he accidentally broke its leg. When the bone snapped, a spot appeared on the iris of the owl's eye. The discoverer of this alleged phenomenon was said to have been 7 years old at the time. Later he studied medicine and, remembering his experience, began to gaze into the eyes of his patients. Books and charts and other material have been prepared on this subject. It goes hand in hand with spinal adjustment as the preferred method of "cure."

BONE HEALING MISINFORMATION

To the Editor:—*A nonmedical unofficial source states that fractured bones will not heal in the Aleutians. Is this true?* *M.D., South Carolina.*

Answer.—The Aleuts are native to the Aleutian Islands and were the only residents of the Aleutian peninsula prior to explorations of the Russians. Now the population is made up of pure-blooded Aleuts, some half-breeds, and, of course, Caucasians who live in the area. The bone physiology of the Aleuts is no different than that of the Eskimos farther north or the Indians in the interior. A practitioner in Alaska has never seen or heard of a case of bony nonunion in natives or Caucasians who have lived in the Aleutians. The same factors that may produce delayed union and nonunion govern healing here.

STERILIZING THERMOMETERS

To the Editor:—*Please give instructions for sterilizing thermometers, oral and rectal, used daily in general practice. What methods are considered adequate?*

Erwin Steinman, M.D., Washington, D. C.

Answer.—Disinfection of clinical thermometers, oral and rectal, may be accomplished by storage in ethyl or isopropyl alcohol, approximately 85% by volume, in a matter of minutes, providing gross contaminants of mucus and feces have been removed. A longer exposure interval is required if tubercle bacilli are among the bacterial contaminants. The solution should be changed frequently enough to keep the concentration in the effective range.

WASHINGTON NEWS

Congress Increases HEW Money . .
Sessions on Problems of Aged . .
Report on Incidence of Poliomyelitis . .
Government Workers' Health Insurance . .
New Housing Bill . .
Joint Council on Aged Meets . .

HEW APPROPRIATIONS TO WHITE HOUSE

Congress completed action on a 3.9-billion-dollar appropriations measure for the Labor Department and the Department of Health, Education, and Welfare and sent the legislation to the President's desk. The bill carried more funds than originally approved by the House but less than a Senate version. However, the total was still 260 million dollars more than the administration had requested, with the bulk of the increase being for health research and hospital construction.

The National Institutes of Health, a branch of the HEW's Public Health Service, received 400 million dollars for its medical research activities, 105 million dollars more than sought by the administration.

The lawmakers approved $186,200,000 for the federal Hill-Burton program of providing grants to states for hospital construction, with the states matching the federal outlays. This was 85 million dollars over the budget figure.

Here is what the various institutes that make up the National Institutes of Health received under the bill:

General Research and Service, $45,900,000; Cancer, $91,200,000; Mental Health, 68 million dollars; Heart, $62,200,000; Dental, 10 million dollars; Arthritis, $46,800,000; Allergy, 34 million dollars, and Neurology, $41,500,000.

CONCLUDE HEARINGS ON PROBLEMS OF AGED

The special Senate labor subcommittee looking into problems of the aged wound up a series of fact-finding sessions here and made plans for hearings in various cities of the country this fall.

The subcommittee, headed by Sen. Pat McNamara (D., Mich.), heard administration officials and spokesmen for national organizations outline their activities.

Testifying for the American Medical Association was Dr. Frederick C. Swartz, Chairman of the A. M. A.'s Committee on Aging. He declared that "solutions are being found, that real progress is now being made through the cooperative efforts of private citizens."

"At this time," he said, "retirement villages, new nursing homes, chronic-disease care centers, home-care programs, recreational facilities, and research projects are being set up from coast to coast—and in substantial number. Furthermore, many, many more are on the way."

Dr. Swartz testified that compulsory retirement ages have much to do with health; he said he has seen many cases in which lack of useful activity has caused older persons to suffer psychologically and physically. "Personnel policies should be flexible enough . . . to use the yardstick of ability instead of the yardstick of age," he said.

Noting that each year more and more of the Americans who are reaching the age of 65 are covered by private, voluntary health insurance, Dr. Swartz said "the problem of financing health services for the aged is therefore a temporary, not a permanent one."

The percentage of senior citizens who need and want health insurance will increase until three-quarters will be covered in 1965 and 90% in 1970, he testified.

Other witnesses, including spokesmen for the Communications Workers of America and the United Steelworkers, also spoke against compulsory retirement ages. Senator McNamara declared that older persons should be included in the main stream of social and economic life.

POLIOMYELITIS INCIDENCE CONTINUES HIGH

The Public Health Service reported that cases of poliomyelitis were continuing to run much higher than last year but that the steep rise during the week ending July 18 appeared to have slackened. For the week ending July 25, 278 cases, including 177 paralytic cases, were listed. This compared with 257 cases in the previous week, of which 166 were paralytic.

For the latest period only the middle Atlantic states showed a sharp rise, due to widely distributed cases in Pennsylvania. PHS said clusters of cases were appearing throughout the country, with no signs of a new epidemic such as occurred in Des Moines, Iowa, and Kansas City, Mo., earlier this year. In contrast to last year, the service said, cases are occurring not only in slum areas but in other districts as well, notably two outbreaks focused around military reservations in North Carolina.

(Continued on next page)

Through the 29th week of 1959 the cumulative total was 1,740 cases, with 1,133 paralytic. Last year the comparable total was 912 total cases. States having highest incidence of poliomyelitis were listed as Iowa, Missouri, Alabama, Texas, Arkansas, South Dakota, and Oklahoma.

HOUSE HEARINGS ON FEDERAL EMPLOYEES' HEALTH BILL

The House Post Office and Civil Service Committee was scheduled to wind up hearings this month (August) on the measure to provide private, voluntary health insurance coverage to the federal government's civilian personnel. Most interested organizations, including the American Medical Association, endorsed the principles of the legislation that won top-heavy approval in the Senate earlier this year.

Administration witnesses also backed the objectives of the legislation, but recommended that the proposed government share of the cost—one-half—be trimmed to one-third, with the employees paying two-thirds. However, the Committee was not expected to change the 50-50 ratio contained in the measure. The program would cost the government about 150 million dollars a year, compared with the 105-million-dollar cost the administration recommended.

The Senate bill does not offer coverage to employees who have already retired, a provision that the A. M. A. has recommended. This is a question of timing, and there is no telling now when these bills will be introduced.

NEW HOUSING BILL CONTAINS NURSING-HOME AID

A Senate banking subcommittee approved new housing legislation that includes some concessions to the protests made by President Eisenhower when he vetoed the housing bill that cleared Congress earlier this session. The new measure, like the old, provides for loan guarantees by the Federal Housing Administration of up to 75% of the cost of proprietary nursing homes.

Also retained in the latest bill were provisions for direct loan authorizations of 25 million dollars for interns' and nurses' housing under the college housing program, cut from $62,500,000 in the vetoed bill, and a 50-million-dollar revolving fund for direct loans to help private nonprofit corporations construct rental housing for the elderly. President Eisenhower objected to the latter provision.

Despite the elimination of some provisions criticized by President Eisenhower, the subcommittee bill calls for almost as much spending as did the original 1.4-billion-dollar measure.

INTERNATIONAL RESEARCH BILL

The administration asked the House to revise a Senate-passed measure establishing a 50-million-dollar program for international research cooperation. Testifying before a House commerce subcommittee, Arthur S. Flemming, Secretary of Health, Education, and Welfare, endorsed the objective of the legislation.

However, he urged that the President, rather than HEW, have direct responsibility for the program, recommended removal of the requirement for a new National Institute of Health, and asked deletion of the 50-million-dollar annual authorization. He said the program should come directly under the President, so it could be coordinated with foreign policy.

The bill would provide a 19-member advisory council with control over financial grants and authorize grants to the World Health Organization and other international groups for research and research training. It contains a specific prohibition against supporting operational public health or medical care programs abroad.

PRESIDENT WELCOMES JOINT COUNCIL SUPPORT

President Eisenhower, in a statement to the Joint Council to Improve the Health Care of the Aged, said the organization's pledge of support to the forthcoming White House Conference on the Aging "is most welcome." The 1961 conference, the chief executive declared, "will require a national effort if it is to achieve its objectives of providing programs to develop the full potential of our older citizens, enabling them to lead useful lives."

The joint council, which held its first official meeting here recently, is made up of representatives from the American Medical Association, the American Hospital Association, the American Dental Association, and the American Nursing Home Federation.

Dr. F. J. L. Blasingame, A. M. A. Executive Vice-president, declared that "with 9% of the nation's population now over 65, this first national conference is significant proof that the physicians of this country, along with hospital personnel, women's organizations, dentists, nurses, religious and labor leaders, industry, and government, are earnestly trying to achieve something worthwhile for America's senior citizens.

"One of our most immediate and compelling challenges is the health care of the aged," he said. "All of us must accept our full share of responsibility in solving the medical socioeconomic issues raised by the ever-increasing number of senior citizens."

At the conclusion of the two-day meeting, attended by 500 persons, representatives of the four sponsoring organizations declared that they are "unequivocally opposed to compulsory government health insurance for any segment of the population."

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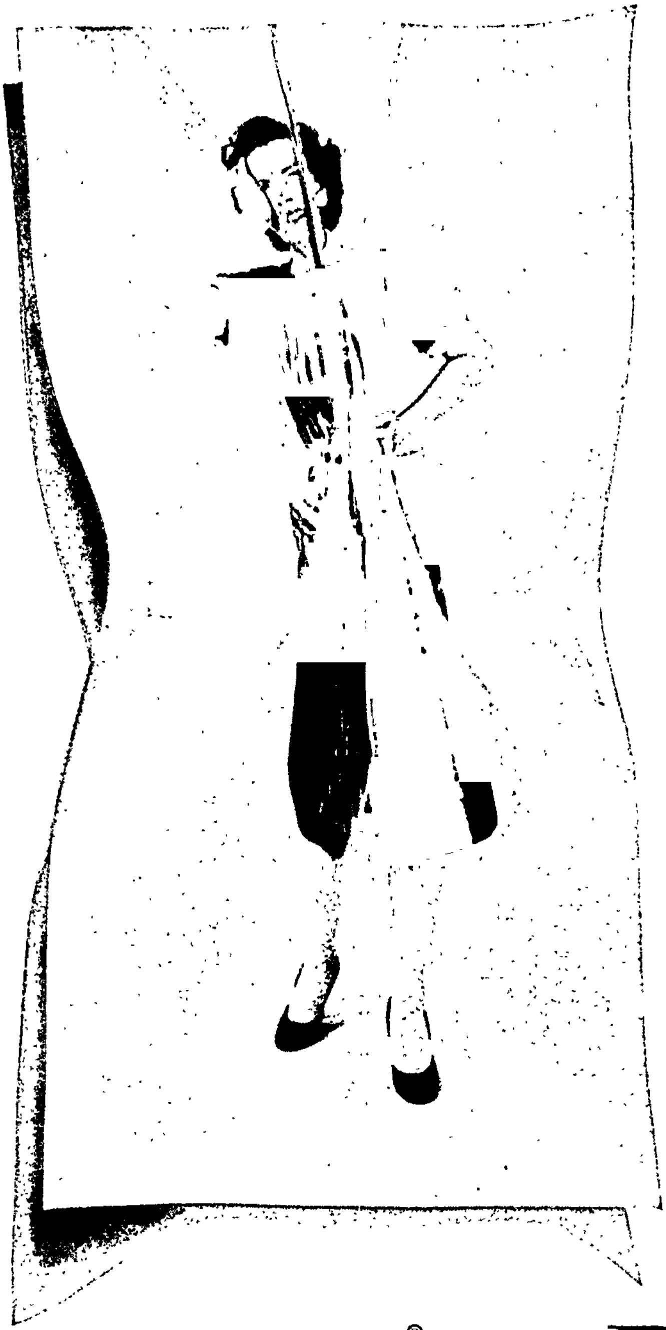

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SEARLE

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 *Clinical Meeting, Denver, Nov. 28-Dec. 1.*
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

August

American Association of Electromyography and Electrodiagnosis, Mayo Clinic, Rochester, Minn., Aug. 29-30. Dr. Edward Lambert, Mayo Clinic, Rochester, Minn., Program Chairman.

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Mississippi Valley Medical Society, Hotel Chase, St. Louis, Sept. 2 Oct. 1. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Il Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. M L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executi Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 2 Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, Th Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeo Chicago, Sept. 13-17. For information write the Secretariat, 1516 La Shore Dr., Chicago 10.

Ohio Society of Anesthesiologists, Dayton Biltmore Hotel, Dayton, Sep 18-19. Dr. Nicholas G. DePiero, 9710 Garfield Blvd., Garfield Ht 25, Ohio, Secretary.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-2 Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executi Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-2 Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Tenn Chairman.

United States Section, International College of Surgeons, Palm House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Sho Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt La City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Sep 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executiv Secretary.

Western Neurosurgical Society, La Valencia Hotel, La Jolla, Calif Sept. 27-30. Dr. Ernest W. Mack, 505 S. Arlington Ave., Reno, Nev Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cleve land, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suit 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, Th Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Sec ond St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, Oc 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hote Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Roo 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hote Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Philadel phia, Oct. 23-25. Dr. Philip Reichert, Empire State Bldg., New York 1 Executive Director.

American College of Chest Physicians, 25th Anniversary Homecom ing Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, At lantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267 Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philadel phia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New Yor 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, Oc 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conra Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lan Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hote Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic Cit N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New Yor 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic City N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, Ba Harbour, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St. Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-17 Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Hote Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray Broadbent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Hotel, Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road, Miami 33, Fla., Executive Secretary.

Association of Clinical Scientists, Sheraton-Park Hotel, Washington, D. C., Oct. 10. Dr. Robert P. MacFate, 323 Northwood Rd., Riverside, Ill., Secretary-Treasurer.

Association of Life Insurance Medical Directors of America, Hotel Statler Hilton, New York City, Oct. 21-23. Dr. Royal S. Schaaf, Prudential Insurance Co., P. O. Box 594, Newark 1, N. J., Secretary.

Association of Medical Illustrators, Seattle, Oct. 5-7. Miss Rose M. Reynolds, University of Nebraska College of Medicine, 42nd Dewey Ave., Omaha 5, Corresponding Secretary.

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STEROID THERAPY AND TUBERCULOSIS

Harry Shubin, M.D., Robert E. Lambert, M.D., Charles A. Heiken, M.D., Adil Sokmensuer, M.D.
and
Allen Glaskin, M.D., Philadelphia

The effect of steroid therapy was investigated in 36 patients with acute and 107 patients with chronic forms of tuberculosis. The steroid used, prednisolone, was added to the regular regimen of streptomycin, isoniazid, and para-aminosalicylic acid. It was started at 50 mg. in divided doses for the 1st day and gradually reduced to 15 mg. by the 23rd day. Two case histories illustrate the recoveries seen in patients with the acute tuberculosis; there frequently was rapid objective improvement, and 32 patients recovered, including 8 with tuberculous meningitis. Two further case histories illustrate the striking results in chronic tuberculosis. The group of 107 included 20 patients who had been expected to die, and 15 of these recovered. The beneficial use of corticosteroids in the treatment of many diseases is well accepted, but the fact that it can reactivate tuberculosis is ofttimes overlooked. A typical case history illustrates such reactivation during treatment of lupus erythematosus with corticosteroids.

PROGRESS in medicine throughout the world has been greater during the past 20 years than in any other period. The discovery of penicillin was closely followed by the isolation of streptomycin, which opened a new era of chemotherapy in infectious diseases. The use of para-aminosalicylic acid (PAS) and isoniazid with streptomycin allowed us, for the first time, to effectively treat tuberculosis. Although the decrease in the death rate from tuberculosis has been marked, many serious problems must be solved if we hope to eradicate this disease.

Within the past 10 years, another distinct advance in medicine was established. This involved the corticosteroid drugs and their relationship to the "stress mechanism," inflammatory and allergic reactions. Their clinical effects in rheumatoid arthritis,[1] lupus erythematosus, and allergic manifestations including bronchial asthma have been well established.

Our interest in the corticosteroids began in 1954, as adjunct therapy in tuberculosis. Fully realizing that laboratory reports[2] showed reactivation of latent tuberculosis by these drugs, our first studies were on terminal cases. Since many of these patients had consistently low 17-ketosteroid levels, it was felt that a state of adrenal insufficiency existed,

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From Philadelphia General Hospital, Northern Division, Rush Hospital, Germantown Hospital, and Wolffe Hospital.

Read before the Fifth International Congress on Diseases of the Chest, Tokyo, Sept. 11, 1958.

either acute or chronic. Therefore, replacement therapy with corticosteroids seemed indicated. When these preliminary findings proved impressive,[3] expanded studies were made with many similar good results.[4] Our early studies indicated the dangers of steroids when the patient had drug-resistant organisms with rapid spread, so that patients' conditions were thoroughly evaluated before treatment was given.

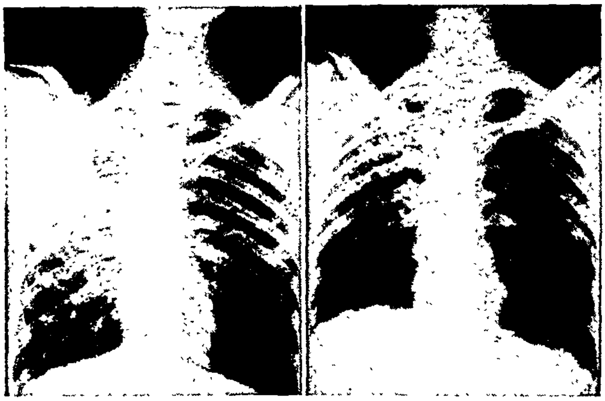

Fig. 1 (case 1).—Roentgenograms taken before prednisolone therapy was started (*left*, Nov. 8, 1957) and after 27 days of therapy (*right*, Dec. 5, 1957), showing extensive clearing of tuberculous lesions.

During this study, we also became increasingly concerned with the reactivation of latent or unrecognized tuberculosis in patients receiving steroids for nontuberculous diseases.[5] Although this number is relatively small in proportion to that of the general use of steroids, these patients are seen with increased frequency by chest specialists and physicians in other fields of medicine should be aware of this possibility.

Plan of Study

This report is concerned with the use of steroids in tuberculosis and their abuse when tuberculosis is reactivated after they are given in treatment of other diseases. The first group consisted of 36 patients with acute forms of tuberculosis, including miliary (14), meningeal (11), pneumococcic (9), and glandular (2), and a total of 107 patients with chronic disease (many with controls)—20 with terminal disease, 21 with allergic reactions to streptomycin or isoniazid, and 66 with pulmonary tuberculosis, moderately or far advanced, who were no longer responding to chemotherapy. We also included six patients with proved sarcoidosis (Boeck's sarcoid) and pulmonary involvement.

Evaluations before and during treatment included physical examinations, routine x-rays monthly, routine blood cell counts, blood chemistry, urinalysis, and determination of 17-ketosteroid level. The latter, together with electrolyte studies, glucose tolerance tests, and the Thorn test, is not now done routinely but only when indicated. Dosage, as in previous reports,[4c] usually was started at 50 mg. of prednisolone (Sterane) in divided doses for the 1st day and was gradually reduced to 15 mg. by the 23rd day.

Acute Tuberculosis

There were 4 deaths in the group of 36 patients with acute tuberculosis. One of these patients was proved at autopsy to have encephalitis, while the other three died shortly after admission (one with staphylococcic pneumonia, one, within 24 hours, with pneumonic tuberculosis, and one, within 72 hours, with meningeal tuberculosis), before adequate therapy could be given. Of the remaining 32 patients, in 14 with miliary tuberculosis and 4 with early meningitis toxicity disappeared within 48 hours, rapid clearing was seen on x-ray examination, and no residual complications occurred. Eight patients with tuberculous meningitis had an excellent recovery, and eight patients with tuberculous pneumonia showed rapid clearing. Two young girls with acute, toxic, tuberculous, cervical lymphadenitis showed almost complete resolution within 10 days after steroid treatment and chemotherapy were started and did not require operation. All patients received streptomyclidene isonicotinyl hydrazine sulfate (Streptohydrazid), streptoduocin (Distrycin), streptomycin, PAS, and/or isoniazid in addition to prednisolone. The following case histories are typical of patients in this group.

Case 1.—A 25-year-old man (fig. 1) was admitted to one of our hospitals on Nov. 7, 1957, with a diagnosis of acute tuberculous pneumonia involving two-thirds of his right lung with bronchogenic spread to his left lung. Toxicity was noted, and a sputum culture was highly positive for acid-fast bacilli. Triple drug therapy (streptomycin, isoniazid, and PAS) was started, but there was no improvement after eight days. Prednisolone therapy was started on Nov. 16, 1957, and marked clinical improvement and extensive clearing, seen on x-ray, occurred in 19 days (fig. 1). Prednisolone therapy was discontinued on Jan. 16, 1958, after the dosage had been gradually reduced, and at this time he had gained 22 lb. (10 kg.) and sputum cultures were negative.

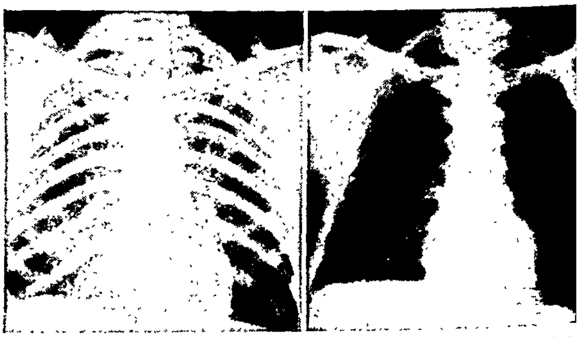

Fig. 2 (case 2).—Roentgenograms taken before prednisolone therapy was started (*left*, Sept. 30, 1957) and after three and one-half months of therapy (*right*, March 17, 1958), showing complete clearing of miliary tuberculosis.

CASE 2.—A 30-year-old man was hospitalized on Sept. 29, 1957, with diagnosis of miliary tuberculosis. His sputum was positive for acid-fast bacilli. He was placed on therapy with the three drugs (including 1,200 mg. of isoniazid daily). There was only slight improvement after two months of therapy. On Nov. 27, 1957, prednisolone was added to this regimen, and marked clearing on x-ray and definite clinical improvement occurred. Sputum cultures became and remained negative. Prednisolone was withdrawn on Feb. 13, 1958, and by March 17, 1958, there was complete clearing of his miliary tuberculosis (fig. 2).

Chronic Tuberculosis

A group of 107 patients had chronic pulmonary tuberculosis moderately or far advanced, and these cases were divided into three classes: (1) terminal, (2) allergic, and (3) active with no response to drugs.

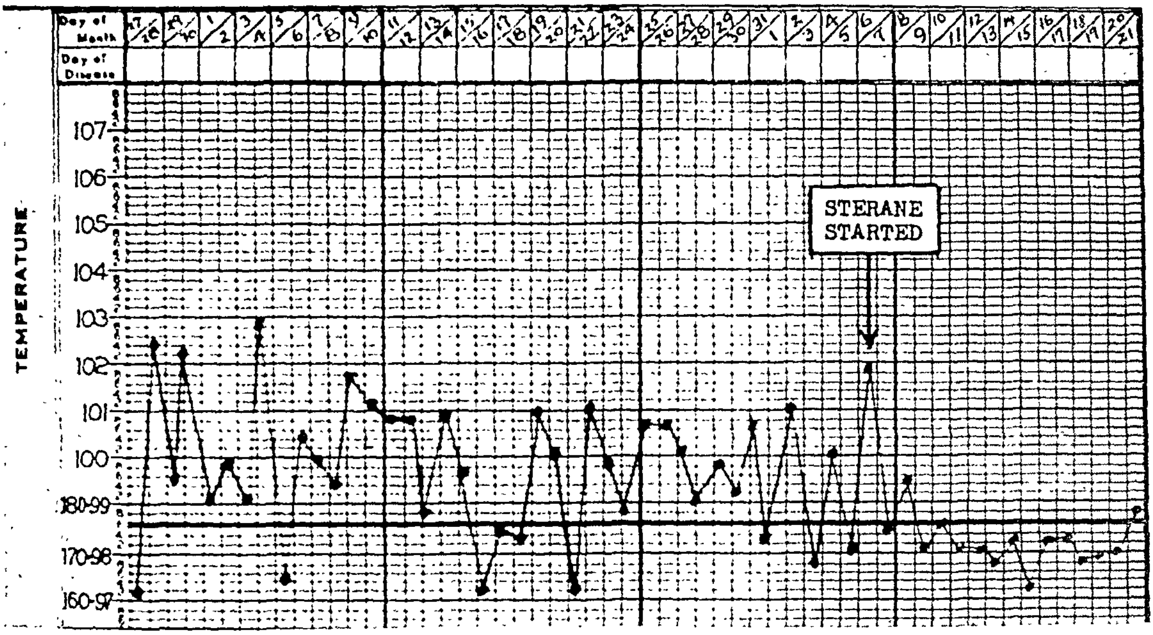

Fig. 3 (case 3).—Temperature chart of patient with far-advanced bilateral pulmonary tuberculosis before and during prednisolone therapy.

Terminal.—Twenty patients with terminal disease received steroids early in their treatment or later as a lifesaving measure. Some, who were in our original treatment group, were practically moribund when steroid therapy was started. Although there were five deaths, it was felt that the remaining 15 patients would also have died had it not been for use of prednisolone. Following is a typical case history.

CASE 3.—A 42-year-old man was admitted to one of our hospitals on Sept. 9, 1957, with far-advanced bilateral pulmonary tuberculosis and sputum positive for acid-fast bacilli. Toxicity was evident, with temperature of 105 F (40.5 C) daily, profuse perspiration, and delirium, and the case appeared to be terminal. He was placed on triple drug therapy. No improvement was seen clinically or by x-ray after one month, and toxicity was still present. There was little, if any, change after two months of triple drug treatment, so he was placed on prednisolone therapy on Nov. 7, 1957. Two days later, his temperature became normal for the first time since admission (fig. 3). By March 11, 1958, there was marked clinical and x-ray improvement (fig. 4), negative sputum cultures, and a weight gain of 20 lb. (9.1 kg.).

Allergic.—There were 21 patients who had allergic reactions to either streptomycin or isoniazid, all of whom still required chemotherapy. Desensitization with gradually increasing dosage, together with steroid therapy, was successful in all but one of these patients. She continued to show allergic reactions, could not tolerate any drugs, had a massive hemorrhage, and died. The other death occurred within 24 hours after operation. Prednisolone therapy had been discontinued five weeks prior to operation, and the patient had received no prednisolone before or after operation. This illustrates the definite need for steroid therapy in any patient who receives these drugs within one year prior to operation or in the presence of infection. In the remaining 19 patients, desensitization was accomplished and 7 had successful operations.

Active with No Response to Drugs.—Patients with resistant, chronic tuberculosis, who have apparently achieved their maximum improvement with present-day antituberculosis therapy, form a serious public health problem. The 66 patients in this group still had evidence of active disease with cavitation or positive sputum findings, although clinically many did not show toxicity. Several factors must be recognized in analyzing such cases: resistance of the tubercle bacillus to available drugs, poor host resistance, and possible chronic adrenal insufficiency. We believed that steroid therapy could not alter bacterial resistance but that some changes might occur. Every means to improve host resistance was used, such as adequate diet, supplemental vitamins, and adequate rest, with no further improvement. The possibility of chronic adrenal insufficiency, verified by low 24-hour urine levels of 17-ketosteroids, was considered a probable indication for steroid therapy. Although the *modus operandi* is not definitely known, we did see improvement in 36 of these patients, 4 of whom had successful operations. The remaining 24 showed no change, either clinically or by x-ray, and 6 died. The following case report is typical of this group of patients.

Case 4.—A 53-year-old man was hospitalized on Jan. 30, 1957, with a diagnosis of far-advanced active bilateral pulmonary tuberculosis. Because of toxicity and extensive disease, he was given triple drug therapy. On June 19, 1957, after almost six months' treatment, there was only slight improvement, with partially resistant organisms. At this time, prednisolone was added to the regimen. There was marked clinical improvement with extensive clearing seen on x-ray by Aug. 15, 1957 (fig. 5). One week later, artificial pneumoperitoneum was started, and on Oct. 3, 1957, his sputum cultures became and remained negative. During the first six months of treatment, he had gained 4½ lb. (2 kg.), but during the six months on prednisolone therapy he gained 25 lb. (11.3 kg.). At the time of writing he is being considered for operation.

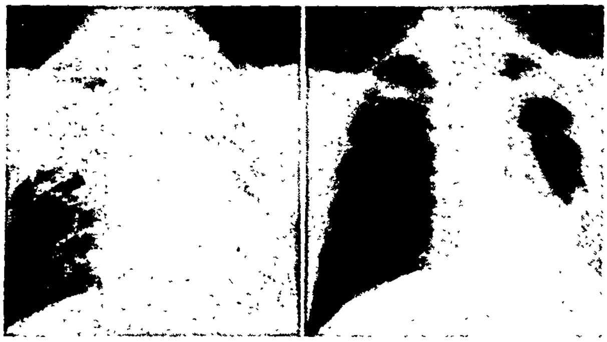

Fig. 4 (case 3).—Roentgenograms taken before prednisolone therapy was started (*left*, Nov. 4, 1957) and after four months of therapy (*right*, March 11, 1958), showing extensive clearing.

Sarcoidosis

Six patients with proved cases of sarcoidosis were included in this study. One also had pulmonary tuberculosis, and all had acute pulmonary involvement due to sarcoidosis. Because of a possible relationship to tuberculosis, all patients were put on the prednisolone regimen with antituberculous therapy. There was excellent resolution in all patients, with marked improvement in the dyspnea of two. In view of the indefinite etiology of sarcoidosis,[6] it is our belief that steroids should be used in the acute manifestations of this disease. At present, the use of para-aminobenzoic acid is being evaluated by Dr. Chris Zarafonetis at Temple University School of Medicine.[7] To date, his results have been interesting, showing that resolution occurs more slowly and that this preparation may be less toxic. Possibly a combination of the two drugs might be of value, and this will be investigated.

Reactivation of Tuberculosis

Just as therapy with antibiotics has been complicated by side-reactions, that with corticosteroids has also produced reactions which could diminish its usefulness. One must always remember that potent drugs, while effectively controlling and curing certain diseases, can also be dangerous by altering other physiological or chemical body functions. The successful results in the treatment of rheumatoid arthritis, bronchial asthma, nephrosis, lupus erythematosus, and other diseases are apparently due to the nonspecific, antirheumatic, anti-inflammatory, and antiallergic activity of the steroids. Although many of the electrolyte changes, fluid retention, gastric ulcers, and blood changes seen with use of the original cortisone drugs are not common with the prednisolone compounds, serious side-effects can still be seen.

As chest specialists, we have been seeing an increasing number of patients with reactivated pulmonary tuberculosis who have received steroids for a variety of diseases. During the past year, we have seen 58 patients in whom active tuberculosis developed during or after steroid therapy without antituberculosis drugs. These patients had been treated for the following diseases: rheumatoid arthritis (16), bronchial asthma (15), sarcoidosis (7), periarteritis nodosa (1), lupus erythematosus (8), allergic dermatitis (5), adrenal cortical hypofunction (1), ocular diseases such as uveitis (4), and polycythemia vera (1).

Only such a small number of such reactivations, compared to the large amounts of steroids being used, would not be serious. However, it is our belief that many, many more "breakdowns" occur which are not recognized or treated. The following case history is typical of this complication of steroid therapy.

Case 5.—A 57-year-old man was first hospitalized on Nov. 15, 1956, with migrating arthralgia, hepatomegaly, and rash, and a definite diagnosis of lupus erythematosus was given. He received hydrocortisone alternately with ACTH. There was a total of four hospital admissions for exacerbations of the lupus erythematosus, which always responded to steroid therapy. His last discharge was on Jan. 12, 1958, and he was readmitted on Feb. 28, 1958, with anorexia, productive cough, occasionally blood-tinged sputum, and weight loss. Reviewing his x-rays, we found that the one taken on Oct. 4, 1957, appeared to be within normal limits (fig. 6 *left*), but there were early changes in the left upper lobe on Jan. 5, 1958. However, this was not at the time considered significant. A roentgenogram taken Feb. 25, 1958, revealed extensive pulmonary tuberculosis with cavitation involving the left upper lobe, with spread (fig. 6 *right*). He was admitted to a tuberculosis sanatorium for further care.

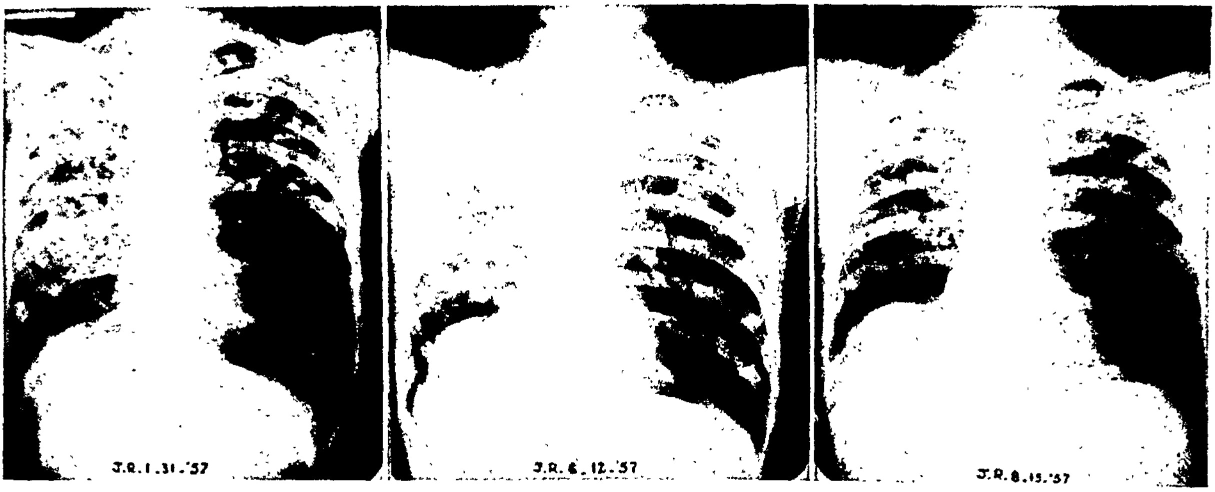

Fig. 5 (case 4).—Roentgenograms of patient with active tuberculosis no longer responding to present-day drugs, showing progressive improvement after institution of prednisolone therapy (*left*, Jan. 1, 1957; *center*, June 12, 1957; *right*, Aug. 15, 1957.

It is not the purpose of this presentation to discourage the use of steroid therapy. However, we urge all physicians using these drugs to investigate the presence of tuberculosis by skin test and x-ray and, if in doubt, to administer simultaneously the antituberculous drugs.

Other studies reveal that the anterior pituitary gland secretes about 1 unit of ACTH daily,[8] while the average daily output of hydrocortisone from the adrenal cortex varies between 12 and 20 mg. Most steroid therapy is given in doses far in excess of normal secretion. When such doses are given for periods exceeding 10 days, a relative suppression of adrenal function occurs. Many investigators, especially Lurie and co-workers,[2] have shown experimentally that excessive doses of cortisone have an adverse effect on tuberculosis. While the newer, more powerful analogs of cortisone, prednisone, and prednisolone are popular because they produce fewer side-effects, they are equally or even more dangerous when excessive dosages are used.

Comment and Conclusions

We are fortunate to be practicing medicine at this time, when so many effective drugs are at our disposal. The value of chemotherapy in the management of tuberculosis has been extensively shown. Steroids also have a place, when used in conjunction with chemotherapy, in the control of certain tuberculosis problems. They can be lifesaving in many acute forms of tuberculosis, are of great value in desensitizing patients allergic to drugs, and are helpful in many patients with chronic, resistant disease. They are also beneficial in treatment of patients with acute sarcoidosis (Boeck's sarcoid) with pulmonary involvement.

The use of steroids in other diseases, such as rheumatoid arthritis, bronchial asthma, and lupus erythematosus, has produced excellent results. There has, unfortunately, been an increasing number of these patients with reactivated pulmonary tuberculosis. Only when these drugs are used judiciously, that is, the minimum dosage for the shortest period necessary to obtain the desired effects, are complications diminished. Intensive skin testing and chest x-ray of every patient receiving steroids, with simultaneous chemotherapy when in doubt, will tend to safeguard against tuberculosis reactivation. These findings illustrate the paradox that a powerful drug can produce disastrous results when used where indicated and yet can produce beneficial results when used where contraindicated—but used wisely.

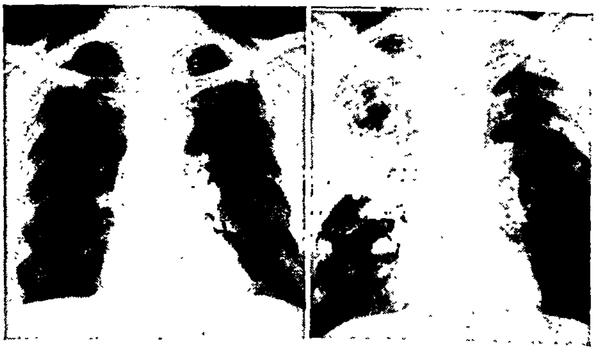

Fig. 6 (case 5).—Roentgenograms of patient with pulmonary tuberculosis reactivated by steroid therapy (*left*, Oct. 4, 1957, *right*, Feb. 25, 1958).

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The prednisolone used in this study was supplied as Sterane through Dr. Kenneth Dumas of Chas. Pfizer & Company., Inc., Brooklyn, N. Y.

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ACCURATE PREGNANCY TESTING IN TRANQUILIZED PATIENTS

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The reported occurrence of false-positive results of pregnancy tests in patients taking certain tranquilizers has been investigated. The test in question involved the intra-abdominal injection of a urine concentrate from the patient into male frogs, and the production of spermaturia constituted a positive result. The 50 psychiatric patients in the present study were all receiving promazine, prochlorperazine, or perphenazine daily in substantial doses. Samples of serum were obtained for use in place of urine concentrates. Hyaluronidase was injected with the serum to facilitate adsorption. Two frogs weighing from 25 to 50 Gm. were used for each of the 50 tests. There was no evidence that the test carried out in this way would give false-positive results in patients receiving tranquilizers of the phenothiazine group.

In 1957 Foxworthy and Lehman [1] reported 75% false-positive results in pregnancy tests performed on male frogs with urine from nonpregnant patients receiving promazine (Sparine) hydrochloride. The total number of tests in their series was not stated. The urine was concentrated by the kaolin adsorption method. The use of serum for pregnancy testing was not discussed in this study.

In the past five years I have performed 1,100 pregnancy tests with Rana pipiens frogs with use of serum exclusively. The accuracy and the many advantages of serum as compared to urine in this method of pregnancy testing have been described in previous articles.[2] In spite of the fact that the use of phenothiazine compounds by the general public has markedly increased, I have not observed any false-positive reactions that might have been attributed to these drugs. It seemed of interest, therefore, to perform according to my method a series of pregnancy tests with serum from patients receiving large doses of perphenazine (Trilafon), promazine, chlorpromazine (Thorazine) hydrochloride, and related compounds, in an attempt to verify the findings of Foxworthy and Lehman.

Method

Tests were performed with Rana pipiens frogs weighing from 25 to 50 Gm. Proper care and refrigeration of the test animals were considered of prime importance.[3] For each 10 Gm. of frog body weight 1 ml. of serum was injected. Prior to injection 1 ml. of hyaluronidase (Wydase, stabilized solution containing 150 U. S. P. units per milliliter) and 3 ml. of sodium chloride solution were added to the serum as a diluent in order to hasten adsorption and prevent anuria.[2a] Injections were intraperitoneal. Two animals were used in each test. As I have found no seasonal variation in the reactivity of these animals, provided they are healthy, the tests were performed throughout the 12 months of the year.

From the Charles T. Miller Hospital.

Serums were obtained from 50 hospitalized psychiatric patients, both male and female, who were taking varying dosages of phenothiazine compounds: 17 were receiving clinical doses of chlorpromazine, ranging from 150 to 400 mg. per day; 26 were receiving promazine, in doses from 75 to 500 mg. per day; 5 were receiving prochlorperazine (Compazine), 60 mg. per day; and 2 received perphenazine, 12 to 20 mg. per day.

Interpretation of "Positive" Tests.—The criterion that Foxworthy and Lehman[1] used for a positive test was a low-power field loaded with actively motile frog sperm. In my laboratory the presence of even one or two spermatozoa constituted a positive reaction, although such would be described as a very weak positive reaction. When a response is weak it will often be noted in but one test animal, presumably the one with the greater reactivity. In such instances, in clinical testing apart from the present series, the test will be repeated in three or four days with subsequent clarification of the clinical problem. The weakly positive responses are usually explained by a subsequent abortion or by an extremely early stage of pregnancy, both of which conditions are characterized by low titers of chorionic gonadotropin. In two tests performed apart from the present series a weakly positive response was obtained in two nonpregnant women at the time of ovulation, presumably as a result of the increased luteinizing hormone present at midcycle.

Results

In the 50 serum tests performed there were no strongly positive responses such as Foxworthy and Lehman described.[1] In the 100 test animals used there were two weak spermaturic responses and one moderately strong response. These three "false-positive" responses would have constituted no problem in clinical practice, inasmuch as in each instance the spermaturia occurred in but one of the two test animals, and the test would have been repeated. The association of these three responses with the patients' medication is indeed open to question.

Report of Cases.—A 42-year-old woman was receiving 150 mg. of promazine and 50 mg. of mephentermine (Wyamine) daily. A serum test performed on her third cycle day resulted in one negative response and one weakly positive reaction. In the latter, the frog became very limp but later recovered. In recent Russian experiments[4] spontaneous spermaturia was observed to occur in frogs operated on by Sechenov's method (sectioned anterior to the optic lobes with removal of the anterior brain). According to Davydova's opinion the spontaneous spermaturia occurring in 25 of 115 operated test animals is due to the release of the centers in the cord from the inhibitory influence of the higher nervous centers. This may explain why occasional spontaneous spermaturia occurs when the frogs are in poor condition or in a terminal state.

A 27-year-old woman was receiving 150 mg. of promazine and 37.5 mg. of mephentermine daily. A serum frog test performed at midcycle resulted in one negative and one fairly strong positive response appearing 90 minutes after the injection of serum. This weakly positive response may have been associated with ovulation.

A 27-year-old man in an extreme state of agitation was receiving 300 mg. of chlorpromazine daily. Result of one frog test was negative, and one showed a very weakly positive response (one to two sperm per high-power field) appearing two hours after injection. A third frog test performed with urine concentrate was negative. This patient was tested one week later when his agitation had subsided and the response was negative, although the dosage of chlorpromazine remained unchanged. This positive response could possibly be associated with the patient's state of agitation. The induction of spermaturia in the frog by injection of epinephrine has been pointed out.[4]

Comment

Since the completion of our series an article has appeared by Hilbert[5] in which he reports 43% false-positive reactions in a series of 30 nonpregnant patients receiving promazine and chlorpromazine. These tests were performed with urine specimens concentrated by the kaolin adsorption method. On three of these patients with false-positive results simultaneous serum tests were performed with correctly negative responses. The author speculated as to whether the failure of the serum to result in a false-positive reaction indicated that the substance giving the false-positive result was an excretory by-product found only in urine. Until such a time as the excretory by-products of the phenothiazine compounds are isolated, we can only theorize as to the reason for the spermaturia caused by the injection of urine concentrate.

Most experimental work shows that tranquilizing drugs tend to produce inhibitory effects in the region of the hypothalamus.[6] One can only speculate whether this may be the mechanism for the production of spermaturia after injection of urine concentrate from tranquilized patients. It may definitely be concluded, however, that in frog tests performed with serum from patients receiving large doses of promazine, chlorpromazine, and perphenazine, false-positive reactions constitute no more of a problem than in any series of pregnancy tests where the slightest degree of spermaturia is carefully noted.

Conclusions

Foxworthy and Lehman[1] and Hilbert[5] have reported high incidences (75% and 43%, respectively) of false-positive results of tests performed on patients taking promazine or chlorpromazine. These false-positive reactions were obtained in tests with use of urine rather than serum.

I performed a series of 50 frog tests on a similar group of tranquilized patients with use of serum instead of urine. There were no actual positive reactions in the entire series. In 3 of the 50 tests weak spermaturic responses were noted with but one of the two test animals. Subsequent repetition of the tests as well as the use of urine concentrate failed to elicit any further spermaturia, and it was felt that factors other than the tranquilizers were probably involved in the production of these three reactions. In clinical practice a weak response in one frog is not accepted as a positive test but is questioned and repeated. Reactions of this nature should be no excuse for incorrect clinical diagnosis or unnecessary surgery.

False-positive pregnancy tests in tranquilized patients apparently can be eliminated by the use of serum instead of urine, which is an example of another advantage of the use of serum over urine in pregnancy testing.

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The hyaluronidase used in this study was supplied as Wydase by Wyeth Laboratories, Philadelphia.

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MANAGEMENT OF WOMEN WITH POSITIVE VAGINAL CYTOLOGICAL FINDINGS

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The authors have acquired experience with many thousands of cytological examinations of the cervix by obtaining smears from all gynecologic and obstetric patients. They are convinced that every woman deserves a cytological examination on the first visit, regardless of age or whether or not she is pregnant. The evidence indicates that positive cytological findings in the pregnant patient are fully as significant as in the nonpregnant. Punch biopsy is done in all cases of cervical lesions. When a histological diagnosis of intraepithelial carcinoma is made or when there is an unexplained positive smear, a cold conization of the cervix is performed. With the expanding number of such examinations, there are large groups of women who have positive findings on cytological examination and in whom frank malignancy does not exist. Management of these patients looms as the newest challenge gynecology has to meet.

Cervical and vaginal cytological studies are rapidly becoming routine diagnostic procedures in the examination of women. As a result, the group of women with positive findings on cytological examination is increasing in size. The management of this increasingly large group of women presents a new and important problem in gynecology.

When the cause for positive findings is an obvious malignancy, the course of action is fairly well defined; therapy depends on the histological diagnosis and the clinical stage of the disease. However, when the patient with positive findings does not have an obvious invasive cancer, and the cause for the presence of the exfoliated cells in question is unknown, the problem becomes perplexing. Because of the tremendous increase in the number of women having vaginal cytological examinations this problem is one that must be faced frequently. This situation poses the following questions: 1. What further diagnostic studies are indicated at the time? 2. What constitutes adequate observation of this patient? 3. How can the physician convince the patient of the need for long-term, constant, and

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consistent follow-up examinations, so that she will assume the responsibility for regular cytological re-examinations, without at the same time instilling a devastating cancerophobia?

Under the designation of patients with positive cytological findings are included those in whom Papanicolaou stains of smears from the cervix and vagina reveal the presence of exfoliated cancer cells or cells that are suspiciously like cancer cells in some of their morphologic characteristics. In this group would be classes 3, 4, and 5 from Papanicolaou's classification.

Materials and Methods

Our experience with cytological examinations at the University of Miami School of Medicine–Jackson Memorial Hospital is already large and still growing. Cytological examination of women was started in 1952 and expanded gradually. With the beginning of a full-time department of obstetrics and gynecology on July 1, 1955, our activities in the field of cytology increased rapidly. In the Miami area we care for practically all indigent patients who have cancer. At present we examine about 9,000 gynecologic patients cytologically every year. On the staff service we see about 55 patients with new cases of invasive carcinoma and 75 with intraepithelial carcinoma of the cervix each year. Because of our accelerated cytology program we are seeing more early carcinoma and discovering more cases of intraepithelial carcinoma of the cervix. The number of cases detected on our service tripled in each of the first three years of the department's history. One index to the extent of our experience lies in the number of conizations done to establish an exact diagnosis in many patients with positive cytological findings. During 1956 we performed 132 conizations of the cervix; in 1957 the number increased to 173; and in 1958 the number was 213.

Our service to patients and our ability to use our patients with positive findings for investigation have been aided by the establishment of a positive cytology registry[1] supported by the National Cancer Institute. This registry is similar to a cancer registry, containing continuous records of all patients who have positive findings and maintaining follow-up contact with these patients. At present about 720 women with positive findings are registered. The length of follow-up study in some of these cases extends as long as six years. We plan to maintain clinical contact indefinitely with all women with positive findings and thus accumulate a record of the natural history of women who exfoliate abnormal cells. Among the cases under observation are a fairly large number of women with positive findings who as yet have not been demonstrated to have cancer.

Some of the unanswered questions are: What will be the ultimate fate of these women? Must these women be expected to develop cancer of the cervix at a later date? Do women who have positive findings have an increased susceptibility to cancer of the cervix or any other part of the body? We hope that answers will be forthcoming from this study.

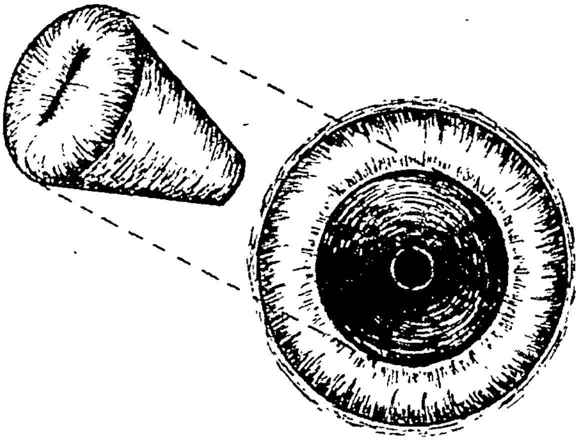
It is our firm conviction that cytological examination of all women is indicated at the first visit, regardless of the patient's age or whether she is pregnant. There appears to be a widespread belief that women below a certain age and women who are pregnant do not need cytological examination. Our experience does not support this contention; it is actually quite to the contrary. One-third of our patients with positive findings on cytological examination are under 30 years of age, and it is becoming clear that just as many women with positive findings during pregnancy have significant cervical disease that needs treatment as do nonpregnant women. Since often the only pelvic examination that many women have is performed when they are pregnant, it would be regrettable if this opportunity to do a cytological study were lost. Some investigators have concluded that cytological examination in pregnancy is not worth while because during this state there are too many misleading cytologists' reports. This also has not been borne out by our experience. We have found that positive findings during pregnancy are fully as significant as at any other time, and these women deserve as much attention as do those who are not pregnant. Since 1955 we have found 28 cases of intraepithelial carcinoma and 6 cases of invasive carcinoma complicating pregnancy. Most of these would have been undetected were it not for our cytology program.

Management of Women with Positive Findings

We interpret as a lesion any grossly visible change from a normal-appearing cervix, including eversion, erosion, cervicitis, or bleeding from any normal-appearing area. Such lesions are excised or sections are taken from them with a biopsy punch for microscopic study. This is done in all cases, regardless of the fact that a smear for cytological study is obtained at the same time. It is imperative to perform biopsies on all lesions, regardless of the availability of smears or the type of smear obtained. The most important reason for this conviction is that some malignant lesions may at times produce a negative result of the Papanicolaou smear.

In a patient who has a lesion a portion of it is excised not only for study but for biopsies. A piece of tissue is obtained from each of the four quadrants of the cervix. In some patients the Papanicolaou smear has given a positive result, but the result of biopsy has been negative for malignancy, the histological examination revealing only cervicitis. In such a situation a cone biopsy and a fractional curettage are done. As seen in the figure each cone biopsy specimen consists of a generous portion of tissue including all of the lesion on the ectocervix and the endocervix for a distance of at least 2 cm. Often the entire endocervical canal is included. To give the pathologist the best possible cone biopsy specimen a cold knife is used, and the hot cautery should not be employed. The cone specimen is obtained before dilatation of the cervix because dilatation can spoil the specimen for the pathologist. The ease with which we do cone biopsy has been greatly facilitated by injection of a dilute epinephrine and saline solution or saline and phenylephrine (Neo-synephrine) hydrochloride solution into the cervix. The hemostatic effect of this solution [2] allows us to obtain a good specimen. The injection of epinephrine does not distort the true histological picture on microscopic examination.

After the cone has been removed the remaining part of the endocervical canal, if any, is curetted. Then the internal os is dilated and the endometrial cavity is systematically curetted. The number of patients with positive findings in whom the results of punch biopsies are negative but cancer is found on cone biopsy encourages us to continue this practice. These cervices heal well without difficulty. Our experience indicates that in about seven weeks the mucosal defect has completely filled in and the cervix is well epithelialized and nulliparous in appearance. The endocervical canal takes somewhat longer for complete healing.



Cone biopsy specimen.

In the case of a patient who has a lesion of the cervix but in whom the cytological smear is negative, a biopsy specimen is obtained at the same time as the smear. If the result of biopsy is also reported to be negative for malignancy we then proceed directly with electrocauterization of the cervix. The cervix is treated with the hot cautery because we believe this to be the most effective therapy for cervicitis. It is also important to use this type of therapy when dealing with patients who are unlikely to return for subsequent clinic visits. Inability to return for prolonged outpatient therapy seems to be characteristic of many clinic patients. Therefore we can give them the best service and care by instituting the most definitive therapy at once. Such patients are asked to return in about five weeks to make sure the cautery has destroyed the lesion and that the tissue has been replaced by normal tissue. If healing is incomplete, the lesion is then cauterized again.

One-seventh of all of our patients with positive findings on cytological examination have no lesion grossly visible on the cervix. When a positive cytological report is received on such a patient, our practice has been to bring the patient back to the clinic as soon as possible and perform quadrant punch biopsies. An endocervical biopsy and endometrial biopsy are sometimes done at that time. If these are negative for malignancy, and cervicitis is the only disease reported, the patient is simply observed. She is seen frequently, at least once a month, and each time a smear is taken. If the repeat smears are negative then we continue to do smears monthly for six months and then every three months for the next six months. If all smears remain negative the patient is returned to the annual cytological examination schedule, which we feel should be a routine procedure for every woman. However, if this patient with a negative result of quadrant biopsy is again noted to have a positive smear on subsequent examination, then a cone biopsy and fractional curettage are done. We are becoming increasingly aware that carcinoma of the cervix may begin in the endocervical canal, beyond the reach of the punch forceps, rather than at the mucocutaneous border.

Appreciation of the origin of the neoplasm in the endocervical canal in many cases and the inconclusiveness of many punch biopsy studies is now changing the above procedure. We are frequently performing a cone biopsy at once when a woman has positive findings and a perfectly normal cervix.

Pregnancy

The pregnant woman with positive findings on cytological examination is approached in much the same way as the nonpregnant patient. For one thing, we frequently deal with women who have never had a pelvic examination and cytological study or at least have not had them for a long time. In such women this may be the only opportunity to detect an important cervical lesion and to cure it. Second, as our experience with the cytological study of pregnant women increases, there is found to be very little difference between pregnant and nonpregnant women, and so it is wisest not to assume that cytological change is due to pregnancy. We have been finding approximately the same incidence of basal cell hyperplasia, intraepithelial carcinoma, and invasive carcinoma among our pregnant patients as in the comparable age groups among the nonpregnant.

In the case of a woman in early pregnancy whose Papanicolaou smear gives a positive result, even if there is no lesion, we do a quadrant biopsy and if it is negative we continue to observe the patient. This means frequent visits and frequent cytological studies. If the quadrant biopsy shows basal cell hyperplasia or intraepithelial carcinoma, or if the positive cytological findings persist, a cone biopsy is performed. Cone biopsies are performed during pregnancy in exactly the same way as in the nonpregnant state. Here again, the injection of a hemostatic solution into the cervix makes the operation simpler. In a patient in advanced pregnancy who is expected to deliver reasonably soon the procedure differs slightly. It is occasionally wise to wait until after pregnancy has terminated before carrying out a vigorous investigation; for one thing, the delay until a definite study is done will not be long, and it may be technically more difficult to excise portions of the cervix in late pregnancy. Our attitude in this regard may change as our experience grows.

We have done 34 cone biopsies in pregnant patients. There is some risk associated with it, but our experience is not large enough to determine the exact extent of the danger. At least two patients have had an abortion soon after conization. The incidence of premature delivery may be significant. It seems that excision of a cone during pregnancy must be considered a calculated risk.

In pregnant patients a quadrant biopsy is done. The bleeding here usually can be controlled by firm pressure with a sponge but sometimes a tampon is inserted for several hours to control the bleeding. One patient had bleeding from a punch biopsy which necessitated her admission to the hospital. If results of the quadrant biopsies are negative the patient is allowed to go on to the point of delivery. In some women at the time of delivery additional biopsy specimens have been taken while the patient is under anesthesia. At delivery the patient is carefully observed by inspection of the cervix and cytological studies. If the smears continue to be positive, a cone biopsy and a fractional curettage are done 12 weeks post partum. This period of 12 weeks is arbitrarily selected and may not have any particular advantages. Many women who have positive findings on cytological examination during pregnancy continue to have them until 12 weeks post partum. If a patient who had positive findings during pregnancy should consistently have negative findings post partum, there may be some rationale for continued cytological observation without more vigorous study.

Women who have positive findings without associated lesions or demonstrable cause or who have intraepithelial carcinoma are allowed to deliver vaginally unless there are obstetric contraindications. Patients who just before term are discovered to have invasive carcinoma are delivered by cesarean section.

Summary

Vaginal and cervical cytological studies are rapidly becoming routine gynecologic diagnostic procedures. With the expanding number of such examinations there are also large groups of women who have positive findings on cytological examination and in whom frank malignancy does not exist. Appreciation of the size of this group and of the ramifications of the problem they present is bound to increase. Management of these patients looms as the newest challenge gynecology has to meet.

This study was supported in part by a grant from the National Cancer Institute, National Institutes of Health.

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MALIGNANT DISEASE AND THE MENOPAUSE.—During this time [the menopause] the individual must make mental and physical adjustments. . . . If she has been sensibly forewarned, so much the better, but unfortunately the mythology concerning the climacteric is still passed on from woman to woman and has survived for so long that many women are reluctant to consult their family doctor about symptoms that are sinister. The practitioner, however, may not be free from blame, for this physiological process too easily becomes a diagnostic wastebin into which various complaints may be discarded. This may mean that symptoms of ominous prognostic significance may be cast aside lightheartedly as all forming part of the "change," the real cause of the symptoms being overlooked. . . . These wrong ideas . . . may lead to diagnostic delays and errors which may cost the patient her health—if not her life. The most obvious example is the supposition that irregular or heavy bleeding about the time of the menopause is to be regarded as a matter of course and only another annoying manifestation of the climacteric.—J. S. Tomkinson, M.B., F.R.C.S., M.R.C.O.G., Malignant Disease and the Menopause, *The Practitioner,* May, 1959.

UTERINE CYTOLOGY—THE "FALSE-POSITIVE" REPORT

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and
Gerald Wilson, M.D., Detroit

Examination of vaginal and cervical smears gives results that generally agree with the result of subsequent study of tissues for biopsy, but occasionally the smear is reported as positive and the biopsy as negative. In a series of 12,885 women there were 100 whose initial cervical smear was reported as positive for malignant cells. In 58 of these the biopsy was positive; in 42 the diagnosis of malignancy was not confirmed by biopsy during the immediate follow-up period. In 37 of the 42 the cause of the discrepancy was found to be an error of sampling or of interpretation. In the remaining five cases no explanation was found.

More than 15 years have passed since the report of Papanicolaou and Traut[1] on the diagnosis of uterine cancer by the vaginal smear was published. In that time there has been abundant confirmation of the fact that it is possible to diagnose carcinoma of the cervix and endometrium by examination of vaginal and cervical smears. Results of treatment for cancer of the cervix, unlike those for carcinomas which develop in many of the internal organs, are easily correlated with the stage of the disease at the time therapy is instituted. Effective means are available for the treatment of early carcinoma of the cervix, and early and adequate treatment for this malignancy should result in the cure of at least 90% of the women afflicted.

Although in general there is excellent correlation between cytological and tissue investigations, a false-positive report of the smear will occasionally appear; that is, the smear will be reported as "positive" and the biopsy specimen as "negative." This is distressing for both the physician and the patient and can cause much anxiety, apprehension, and expense. The study herein reported was begun in an effort to find the ultimate disposition of cases in which there is a failure of correlation of the tissue with the cytopathological diagnosis.

Material and Methods

From Jan. 1, 1956, through Feb. 17, 1958, 12,885 female patients were examined at the Yates Memorial Clinic. Of this group there were 100 patients whose initial cervical smear was reported as positive for malignant cells. Of these patients at the Yates Clinic a positive biopsy report was obtained in 58 within 10 days of the initial examination. For the remaining 42 patients the positive smear was not confirmed on immediate follow-up examination. Efforts were made to reach these patients through their private physicians and to obtain additional tissue which might reveal the presence of malignancy. These attempts were successful in 98 of the 100 patients, there being 2 in whom no biopsy was performed. In addition, all "negative" biopsy reports were reviewed by a panel of three pathologists. The smears from those patients whose diagnosis of carcinoma was not confirmed were reevaluated. It was thought that by these methods it should be possible to define the reasons for the failure of correlation between the cytological report and the initial tissue examination.

Results.—The initial biopsy confirmed the diagnosis of malignancy by cytological examination in only 58 of the 100 cases. The 42 apparent discrepancies were resolved in the following manner: Two patients had cervical biopsy studies done at a clinic other than the Yates Clinic which confirmed the presence of malignancy. For 15 patients the diagnosis of carcinoma of the cervix was established by examination of additional tissue—7 by conization, 7 by hysterectomy, and one by punch biopsy. Of this group five were proved to have invasive carcinoma of the cervix. For four patients the diagnosis of malignancy was not confirmed until it was realized that the carcinoma was not of the cervix but of another site, in three of the endometrium and in one of the vulva. A review of six of the original biopsy studies by a panel of pathologists resulted in a change of diagnosis from "benign, atypical hyperplasia" to "malignant, noninvasive carcinoma." Thus it happened that the positive smear diagnosis was confirmed in an additional 27 cases. Review of the smears resulted in downgrading from "positive" to "atypical" or "suspicious" in eight cases. There were five cases in which the biopsy specimen appeared adequate and benign, and yet the smear was still regarded as positive. The remaining two patients had no biopsy examination.

Comment

There are several reasons for failure to confirm a diagnosis of cancer made by cytological examination of cervical and vaginal cells. Among these are

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From the Yates Memorial Clinic and Wayne State University.

(1) mistaken identity of patient or specimen; (2) improper identification of atypical, degenerated, or otherwise altered benign cells as malignant; (3) failure to perform biopsy; (4) failure to obtain an adequate biopsy specimen; for example, too small a sample, crushed tissue, material from uninvolved area, or carcinoma in tissue not sampled, such as endometrium; (5) improper evaluation of tissue changes in the biopsy specimen; or (6) unresolved problems.

Each reason for lack of correlation was seen in the present series except improper identification. By far the largest group of errors is that listed as failure to obtain adequate material for biopsy. Of the original 42 discrepancies 21 were in this category. The biopsy specimen must be adequate with regard to size, must come from an involved area, and must be handled in such a way as to allow an adequate pathological examination. Tissue which has been crushed or in other ways damaged, so that fine histological detail is no longer discernible, must be considered inadequate. Any burning of the tissue by various types of electrical instruments will render it unsuitable for histological examination. Sometimes the biopsy specimens are too small or are taken from the portio vaginalis when the involved area is near the internal os. A common mistake was made by gynecologists who dilated the cervix and curetted the endometrium before doing the cervical biopsy. Under such circumstances it often happened that the biopsy specimen was inadequate because all of the surface epithelium had been removed from its normal position.

Lest it be thought that all cases which were diagnosed by additional material from the cervix were noninvasive carcinoma, it should be emphasized that of the seven instances in which cold conization of the cervix revealed the malignancy when the punch biopsy specimen had appeared to be nonmalignant four proved to be invasive carcinomas. This is an important consideration, for it is not generally appreciated that one can miss an invasive carcinoma of the cervix by punch biopsy. Of the seven instances in which a hysterectomy changed the diagnosis one was found to be an invasive carcinoma of the cervix. In four cases the biopsy specimen was inadequate because it was of the wrong organ or tissue. Three of these were found to be carcinomas of the endometrium, and the original biopsy specimens were from the cervix. The fourth case was a carcinoma of the vulva. These data emphasize the important part that the clinician plays in ferreting out the cause of the discrepancy between the positive cytological report and the original biopsy diagnosis.

The next largest group of cases in which the discrepancy was resolved was that in which the original cytological diagnosis of a positive smear was incorrect. This happened in 8 of the 100 cases and was revealed when, on review of these smears, it was realized that cell alterations caused by degeneration, improper fixation, and infection had been mistakenly diagnosed as malignant change. The number of these cases should be few and ordinarily will reflect the experience of the cytologist. With better understanding of the cell changes resulting from various benign reactions there should be a reduction in the number of true false-positive smear diagnoses made.

Another facet of this problem which is deserving of emphasis is the matter of evaluation of tissue changes as present in the biopsy specimen. It is regrettable but nonetheless true that the diagnosis of carcinoma in situ is still a subjective matter, to some extent. The definition of noninvasive carcinoma which has been utilized in this study stipulates that the change in the epithelium must be such as to resemble that seen in invasive carcinoma. Since there are several varieties of patterns of invasive carcinoma, it follows that there will be corresponding patterns for intraepithelial carcinoma. Despite wide experience in this area there will be truly borderline cases in which the changes appear to be more than atypical hyperplasia and still somewhat less than noninvasive carcinoma. For this study we have attempted to resolve these problems by having a panel of three pathologists review the sections. The examination of the sections was made independently by the reviewing board and the diagnoses were changed from "benign" to "malignant" only when at least two of the pathologists thought, on review, that the correct diagnosis should be intraepithelial carcinoma. There are pathologists who are unwilling to make the diagnosis of noninvasive carcinoma. All smear diagnoses which are called "positive" because of the presence of exfoliated cells from noninvasive carcinoma will be considered by these pathologists as "false-positives." There is no doubt that we should have a more concise and easily applied definition of intraepithelial carcinoma.

Even after prolonged follow-up study, review of original and additional biopsy material, and reexamination of the cytological smears, there were 5 cases of the 100 which remained unresolved. In these the smear diagnoses were still "positive," but there had not been any histological confirmation. These could properly be considered as cases of unconfirmed positive cytological diagnoses. There was a good deal of anxiety and expense for these patients and their physicians; and, at least to date of writing, there has been no benefit to the patient. Possibly a longer period of follow-up will reveal a malignancy which has not been detected. On the other hand, it may be that these cases are examples of changes within the cells (in the smears) which rarely occur in the absence of malignancy and are indistinguishable from the changes that reflect the development of cancer.

Summary

Results of the first biopsy study at the Yates Clinic of 100 patients with positive cervical or vaginal cytological findings confirmed only 58 of them. All but 5 of the 42 apparent discrepancies were subsequently resolved by study of additional biopsy material, review of the original biopsy studies, or review of the original smears.

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TROPHOBLASTIC PULMONARY THROMBOSIS WITH COR PULMONALE

REPORT OF A CASE DUE TO MALIGNANT HYDATIFORM MOLE OF FIVE YEARS' DURATION

Robert J. Fahrner, M.D., Andrew J. McQueeney, M.D., Jack M. Mosely, M.D.
and
Robert W. Petersen, M.D., Santa Barbara, Calif.

The patient's first pregnancy, in 1953, terminated at five and one-half months with the expulsion of a mass that was described, on the basis of microscopic examination, as a benign hydatiform mole. Five years later, after repeated pulmonary complaints, the patient was found to have infiltration of the left lung field and left pleural effusion. After hospitalization, her condition deteriorated steadily. Postmortem examination confirmed the clinical impression of multiple pulmonary infarction and cor pulmonale. The infarcts were due to choriocarcinomatous tumor thrombi originating from a Y-shaped saddle type of trophoblastic tumor obstructing the pulmonary arteries bilaterally. It is unlikely that administration of chorionic gonadotropin to the patient in the five-year interval for infertility stimulated trophoblastic proliferation, but this possibility cannot be entirely excluded.

Blood vessel invasion by the trophoblastic covering of the ovum occurs normally at the implantation site, and trophoblastic deportation to the lungs is estimated to occur in 80% of normal pregnancies; spontaneous regression is the rule. In the present case, however, angioinvasive trophoblast filled the entire pulmonary arterial tree after malignant transformation of a hydatiform mole of five years' duration. Death was ultimately due to multiple progressive pulmonary infarction and cor pulmonale.

Report of a Case

On March 31, 1958, a 30-year-old woman was admitted to the St. Francis Hospital, Santa Barbara, Calif., with a chief complaint of shortness of breath for one week. History revealed an infertility problem dating back to her first pregnancy, which terminated at five and one-half months, on Oct. 1, 1953, with the passage of a 450-Gm., bloody mass containing numerous grape-like structures having the appearance of typical hydatid-like cysts. The pathological diagnosis of benign hydatiform mole was made on the basis of microscopic examination at that time, but recent reexamination has shown foci of atypical trophoblastic growth on the surface of blood clot (fig. 1).

Dilation and curettage performed on Oct. 5, 1953, was reported as showing "necrotic decidual tissue." A Friedman test was reported to give negative results on Oct. 23, 1953, but doubtful results on Dec. 17, 1953. Chest x-ray on March 30, 1954, was reported to show negative findings.

During the next three years, five subsequent pregnancies, each terminating in a spontaneous abortion before the sixth week, were followed by curettage, and at no time was any molar tissue subsequently identified.

She was referred to one of us (R. J. F.) as having an infertility problem in September, 1956. Clinical and laboratory evaluation was concluded in Decem-

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From St. Francis Hospital.

ber and seemed to indicate a deficiency in progesterone and chorionic gonadotropin. Consequently, a three-month course of hormone therapy was instituted Jan. 17, 1957. Menses remained normal, and with each cycle she received 300 mg. of progesterone orally plus 6,000 I. U. of chorionic gonadotropin (Antuitrin-S). The final course of chorionic gonadotropin therapy was completed on April 8, 1957.

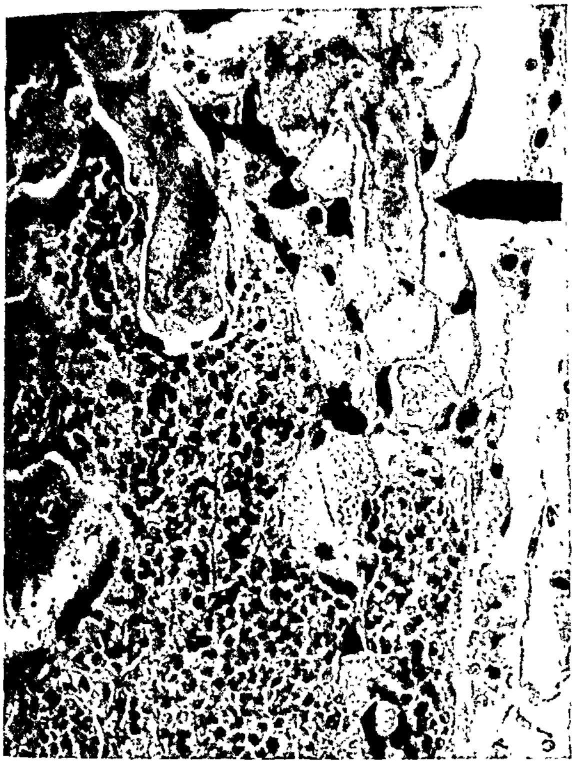

Fig. 1.—Photomicrograph of mole, taken in October, 1953, showing atypical trophoblastic growth on surface of blood clot. Note absence of normal villose stroma (hematoxylin and eosin stain, × 430).

In May, 1957, the patient had an episode of "pneumonia" of two weeks' duration. This consisted of pleuritic chest pain on the right side and fever, together with apprehension and shortness of breath but no hemoptysis. Roentgenogram of the chest revealed an infiltration at the right base.

On June 12, 1957, the patient suspected she was pregnant, and a frog test was reported to give positive results. Chorionic gonadotropin was again administered from the 14th to the 19th of June. Profuse bleeding followed, necessitating dilation and curettage June 25, which revealed, on microscopic examination, "endometrium, proliferative phase; nothing suggesting a recent pregnancy."

In early November, 1957, the patient again had a four-day episode of pleuritic pain over the right side of the chest, associated with cough. On Nov. 20, an endometrial biopsy was obtained and showed benign endometrium in the proliferative phase with focal glandular atypism. Diagnostic dilation and curettage was performed on Dec. 10, 1957, but microscopic examination revealed only "atrophic benign endometrium, proliferative phase, without evidence of atypism." A frog test on Dec. 9 was again reported to give positive results. Chest x-ray on Dec. 10 revealed a normal chest.

In January, 1958, she developed pain over the left side of the chest, breathlessness, and cough, associated with occasional hemoptysis; she was hospitalized at that time because of infiltration in the left lung field and left pleural effusion. Within one week, infiltration became nodular in appearance and more extensive. It was the opinion of the roentgenologist at this time that metastatic disease to the lungs or pleura should be given serious consideration (fig. 2). Because of the pleural effusion associated with this infiltration, tuberculin and coccidioidin tests were performed and gave negative results. Sputum was negative for acid-fast bacilli.

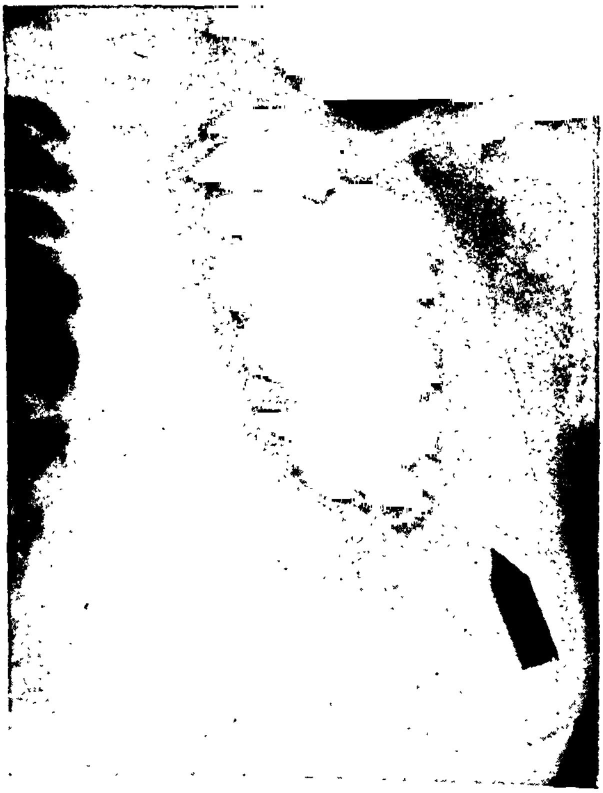

Fig. 2.—Roentgenogram, showing pleural effusion on left with multinodular infiltration.

Chest fluid gave positive findings on a pregnancy test in a 1:5 dilution. The urine pregnancy test likewise gave positive results but only after concentration, indicating a chorionic gonadotropin titer in the chest fluid approximately 250 times higher than that of the urine. At this time, four and one-half years after the molar pregnancy, the quantitative chorionic gonadotropin titer on the urine was only 4,800 I. U. per 24 hours, i. e., less than one-tenth the maximum titer obtained in a normal pregnancy.

In February, 1958, exploratory thoracotomy revealed approximately 20 small, recent, hemorrhagic nodules in the left lung, the majority in the left lower lobe; one of these was excised for pathological examination, which showed a hemorrhagic infarct with no demonstrable metastatic disease. A diagnosis of chorioadenoma was considered, and total hysterectomy and bilateral salpingo-oophorectomy was performed March 12, 1958. The ovaries were not enlarged or cystic, showing, microscopically, a heterotopic decidual reaction but no evidence of excessive lutein response. Pathological examination and careful reexamination failed to show evidence of trophoblastic foci in the uterus or uterine adnexa.

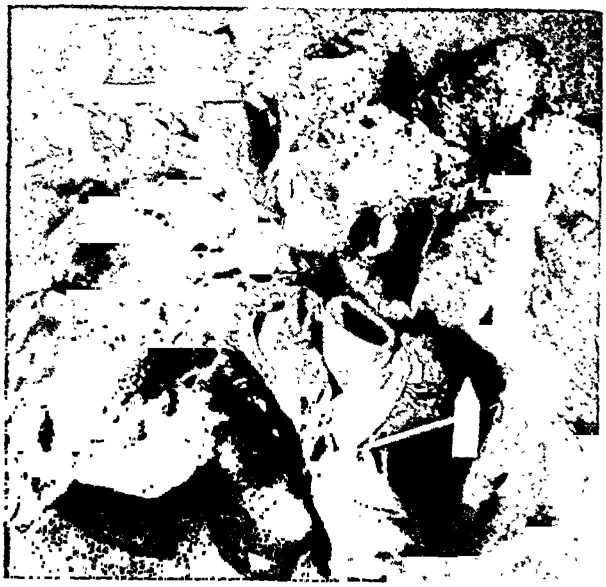

Fig. 3.—Heart-lung preparation with pulmonary conus opened, showing saddle thrombus at bifurcation of pulmonary artery. Note multiple pulmonary infarcts and cor pulmonale.

The patient was readmitted to the hospital on March 31, 1958, primarily because of increasingly severe shortness of breath for the past week, with associated palpitation and a sharp, pleuritic type of chest pain localized just beneath the left breast. She had been coughing up moderate amounts of blood-streaked sputum and had had an intermittent low-grade fever with fairly severe night sweats for the past three weeks. On the day of admission she was dyspneic at rest, and a chest roentgenogram at this time showed tiny multiple nodules and a marked increase in the vascularity of both lung fields, with enlargement of the pulmonary artery segment in the region of the right hilum. Findings were thought to be due to multiple embolic phenomena with associated pulmonary arterial hypertension.

The patient improved slightly on anticoagulant and oxygen therapy, but on April 10, 1958, she complained of increasing dyspnea, became cyanotic, and suddenly died. The clinical diagnosis was multiple pulmonary infarctions, pulmonary hypertension, pulmonary embolism, and cor pulmonale. In spite of the long history, normal pelvic organs, and low chorionic gonadotropin titer, it was felt that these changes were in some way related to the molar pregnancy of October, 1953, four and one-half years prior to death.

Postmortem examination confirmed the clinical impression of multiple pulmonary infarction and cor pulmonale. Pulmonary infarcts originated through propagation of a large, Y-shaped, saddle type of trophoblastic tumor thrombus which was found obstructing the pulmonary arteries bilaterally (fig. 3). The older portion of the saddle thrombus was densely adherent to the posterior wall of the pulmonary artery for a distance of 2.0 cm.; the surface of the thrombotic mass appeared filamentous or

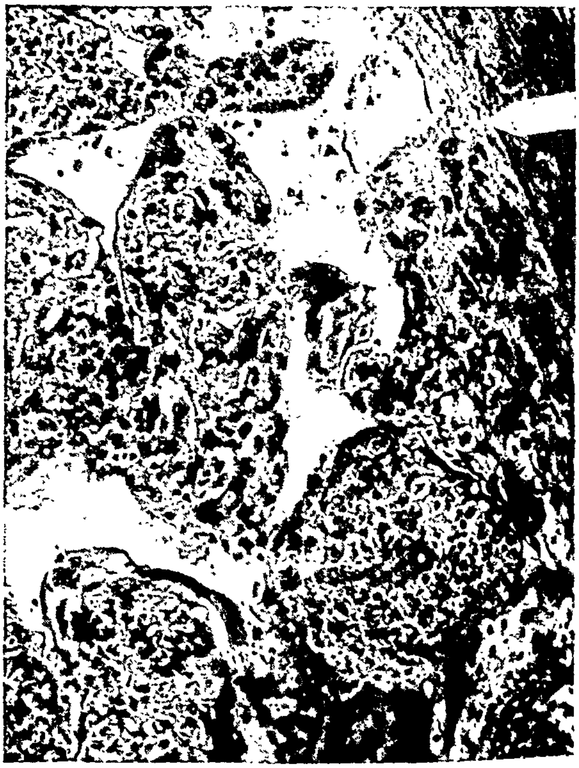

Fig. 4.—Photomicrograph, showing intravascular choriocarcinomatous thrombus within pulmonary infarct. Note absence of villose stroma and fixation to arterial wall, upper right (hematoxylin and eosin stain, × 430).

finely papillary, and the entire thrombus had a spongy, friable consistency, resembling placental tissue. The more recent propagating portions of the thrombus extended into the distal segmental portions of the pulmonary arterial system bilaterally but most marked on the left side. On microscopic examination, the tumor thrombus in the pulmonary artery was largely necrotic, but a thin surface film was formed by trophoblastic elements in an atypical villose pattern; identical thrombi were demonstrated within the more recent pulmonary infarcts (fig. 4).

The heart showed the dilated, hypertrophic right ventricle characteristic of well-established cor pulmonale; there was no evidence of endocarditis or mural thrombosis within the heart proper. The lungs showed multiple pulmonary infarcts, bilaterally, healed, organizing, and recent, with associated acute fibrinous pleuritis in the right upper and lower lobes. Individual infarcts ranged in size from 4 to 6 cm.; there was no evidence of extravascular pulmonary metastasis.

Microscopic examination showed the pulmonary infarcts to be due to multiple tumor thrombosis within segmental branches of the pulmonary arterial system. The arterial lumen in the center of recent infarcts was occluded by choriocarcinomatous tumor thrombi arranged in an atypical villose pattern; individual tumor masses were formed by cytotrophoblast covered by syncytial trophoblast, both appearing hyperplastic and atypical. The normal villose stroma was characteristically absent, but cellular pleomorphism was minimal and mitoses were rare (fig. 4).

No extrapulmonary choriocarcinomatous metastases were demonstrated. Of incidental interest, in view of the obstetric history, was the presence of a small chromophobic adenoma in the anterior lobe of the pituitary gland.

Comment

The occurrence of cor pulmonale due to multiple pulmonary infarcts is well recognized,[1] and two cases similar to the present one have been previously reported.[2] A unique feature of the present case, however, appears to be the bilateral involvement of both pulmonary arteries and their major branches by intravascular tumor thrombosis. The degree of cor pulmonale and the early history of pulmonary infarction confirmed by x-ray examination suggest that unrecognized tumor thrombus was established and propagating within the pulmonary arterial system for at least a year prior to death and probably long after disappearance of the primary uterine tumor. In the clear light of hindsight, a propagating saddle thrombus in the pulmonary artery might have been suspected because of the asymmetrical distribution of the pulmonary infarcts. For example, in one episode all infarcts appeared in the right lung, while in a later episode all infarcts appeared on the left. In contrast, multiple emboli from a peripheral source would more likely be distributed by chance to both lungs equally.

With respect to the malignant transformation of the hydatiform mole, it appears that its malignant potentialities were well established during the molar pregnancy five years before. Hertig,[3] after reviewing this material, called attention to the atypical trophoblastic growth in the original mole, emphasizing again the importance of examining microscopically all associated blood clots as well as molar tissue. This makes it unlikely that the administration of chorionic gonadotropin stimulated or influenced subsequent trophoblastic proliferation, although this possibility cannot be entirely excluded.

With the microscopic findings, the present case provides a kind of "missing link" in the transition from invasive mole to choriocarcinoma. The prominent villose growth pattern (fig. 4) is characteristic of mole, while the absence of stroma within individual villi is an important differential point in favor of choriocarcinoma.[4] It is noteworthy, however, that the tumor remains entirely intravascular, and this absence of invasion beyond vascular channels appears to be a characteristic feature.

Therapeutic management of this young primipara was conservative in line with the original benign tissue diagnosis, but, in retrospect, one must recall the comment of Novak and Seah[5]: "To insure removal of the occasional genuine choriocarcinoma, it is necessary to sacrifice a good many uteri harboring lesions which are not malignant and would usually regress and disappear."

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CONTROL OF TETANUS SPASMS BY ADMINISTRATION OF MEPROBAMATE

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The course of tetanus has been studied in 39 patients treated with meprobamate. Among the 20 who were addicts to heroin (diacetylmorphine) there were 14 deaths; of the 19 nonaddicts only 4 died. Morbidity has been greatly reduced. Before the introduction of the meprobamate treatment, in a group of 51 patients there had been 33 deaths, 26 being among the 36 heroin addicts in the group. While the mortality among the heroin addicts remained the same, mortality among the nonaddicts was strikingly reduced by the use of meprobamate. In most patients, complete control of somatically induced seizures was attained by giving 400 mg. of meprobamate in 5 cc. of polyethylene glycol intramuscularly every four hours. Two case histories illustrate its effects, which are manifest within 15 minutes and last three or four hours after each injection.

In spite of the widespread use of tetanus toxoid in pediatric immunizations and in Army inductees, tetanus is still prevalent in certain areas of the United States.[1] At the Cook County Hospital in Chicago there have been approximately 20 to 25 cases a year. In India, Africa, the West Indies and South America,[2] and other areas of poor medical hygiene, the disease is extremely common. As a result of the use of antibiotics, tracheotomy, intravenous feedings, and improved nursing, in the last 20 years there has been a gradual drop in mortality from tetanus in the United States from about 75% to about 25%.[3]

At the Cook County Hospital there has recently been a change in the type of tetanus patients seen. Most of the patients in the past 10 years have been persons addicted to heroin (diacetylmorphine) in whom the disease resulted from use of contaminated heroin. There is usually a rapid onset of symptoms—24 hours or less, and a high mortality—over 90%. The prognosis in tetanus is more closely related to the rapidity of development of symptoms than to any other factor. In general, if the elapsed interval between the first symptom, such as stiff neck or trismus, and the first spasm is less than 24 hours, mortality is about 90%; if this period is between 24 and 48 hours, mortality is about 50%; if the period is between 48 and 96 hours, mortality is about 25%; if it is five days or over, mortality is about 10%. These clinical correlations are the subject of another paper.[4]

Nature of Spasm and Clinical Course

Sherrington[5] pointed out that the seizures of tetanus are physiologically identical with those of strychnine poisoning. In both conditions there is a loss of a reciprocal relaxation and in its place reciprocal facilitation occurs. Thus, any voluntary attempt at motion results in irradiated hyperactivity to the antagonist so that spasms occur primarily in the direction of action of the stronger muscle groups. An attempt to open the jaw results in a facilitation of the more powerful muscles that close the jaw so that the clinical picture of "lockjaw" appears.

These seizures are extremely painful, since the patient is conscious. Because they involve all of the muscles of the body, extensor spasms predominate. The spasms also involve the respiratory muscles and thus predispose to hypoxic episodes and pulmonary infections. In untreated patients these spasms may be sufficiently severe to cause compression fractures of the spine or even rupture of some of the muscles, e. g., rectus abdominis. Because of the increased irritability of the central nervous system, spasms may be precipitated by exteroceptive (somatic) stimuli such as bright lights, noises, pinpricks, or skin pressure. They may be triggered also by proprioceptive stimuli from passive movement of an arm or a leg, as occurs in turning the patient. Interoceptive (visceral) stimuli from gas in the gastrointestinal tract, an overdistended bladder, or mucous plugs in the bronchi may likewise precipitate seizures.

The early and obvious causes of death in patients with tetanus are associated with hypoxia, pneumonia, respiratory spasm, oversedation, exhaustion, shock, and secondary infection. Death from these causes often occurs in the first two to five days. More subtle and often delayed lethal factors are concerned with acidosis, alkalosis, and other electrolyte or enzymatic disturbances. Frequently patients who seem to be improving, insofar as the neuromuscular symptoms of the disease are concerned, may develop cardiorespiratory arrhythmias and high temperatures. This is particularly so in patients with heroin addiction who often die with a syndrome simulating central bulbar involvement. For patients who survive the first week, the prognosis for recovery is good. They generally improve

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gradually but may have residual stiffness for two to six weeks in the muscles of the back, neck, and pelvic and shoulder girdles.

General Management

Due to the many factors involved, the clinical care of the patient with tetanus must embrace several phases. (A more extensive description of the routine treatment of tetanus[6] at the Cook County Hospital is the subject of a separate paper.) This includes the administration of tetanus antitoxin to neutralize circulating toxin; the use of penicillin and other antibiotics for secondary infections; the control of hyperirritability by sedation; the use of oxygen and tracheotomy to maintain respiratory adequacy; steroids for shock; the insulation of the patient from noises, bright lights, or other triggering stimuli; and general hygienic measures.

Tracheotomy has proved to be an important portion of therapy and in itself has been responsible for a reduction in the mortality due to tetanus. Its effectiveness depends not only on maintenance of a free airway but also on reduction of the apprehension and air hunger of patients with respiratory spasms.

Control of Spasms by Drugs

The control and prevention of seizures in patients with tetanus has been one of the most important and vexing problems. The general therapeutic procedures enumerated above fall short of attaining this goal. Drugs and other specific measures hitherto employed to control spasms have been of only moderate benefit and have introduced some additional hazards.

Management of the convulsive phase by sedative drugs has left much to be desired, since barbiturates and similar centrally acting sedatives must often be given to the point of respiratory depression in order to be effective. Deep sedation not only keeps the patient in a state of perpetual coma, thus preventing him from being communicative, but also increases the nursing problems because of the tendency for hypostatic pneumonia and lethal depression of respiration to occur.

From a theoretical point of view, muscle relaxants such as curare and its analogues were promising. Practically, however, they have proved to be ineffective in reducing mortality and morbidity. Curariform drugs, moreover, must be given parenterally. When injected intramuscularly in long-acting wax menstruums, they are ineffective, and therefore the aqueous forms must be given by continuous intravenous drip and to the point of respiratory paralysis. The use of the "iron lung" or of positive-pressure machines for artificial respiration adds not only tremendous obstacles to adequate nursing but also the hazards of the pulmonary complications due to the continued use of such machines. Curare, moreover, does not decrease the apprehension of the patient in spite of adequate oxygenation unless sedatives are simultaneously administered.

Mephenesin, because of its pharmacological action as a muscle relaxant in animals, has been tried and its use discontinued because of practical objections. It has an extremely short duration of effective action and must also be given by continuous intravenous drip and in very large doses. The clinical response of the patient has been disappointing and its effect on mortality and morbidity negligible.

Recently, chlorpromazine and its analogues were added to the list of drugs used to control the spasms of tetanus, and these drugs have been of some value. Chlorpromazine has not, however, successfully controlled seizures unless given to a point of putting the patient to sleep. If it is given for several days, a dangerous depression and fall of blood pressure may ensue. Although the drug has been responsible for giving some comfort to the patient, the side-effects such as hypotension and depression have militated against routine prolonged use in large doses, and it apparently has had no effect on the ultimate outcome of the disease. An advantage of the use of chlorpromazine is that somewhat smaller doses of barbiturates can be given.

In search for a drug which could be used with the assurance of a relatively wide degree of safety and which would control seizures without affecting respiration, blood pressure, or consciousness, we had occasion to use meprobamate (Miltown) intramuscularly. As a muscle relaxant, meprobamate, as compared to mephenesin and curare, has prolonged action. Its effectiveness in safe dosages has been reported by many authors. Our clinical experience with meprobamate in tetanus is presented not only to point out the remarkable effectiveness of the drug on some of the spasms of tetanus but also because our observations may help to elucidate the pathological physiology of tetanus and the pharmacological action of meprobamate.

Present Study

Patient Population.—At the pediatric division of the Cook County Hospital, a tetanus team has existed since 1933. All patients with tetanus coming to Cook County Hospital, whether children or adults, are referred to this service.

While tetanus formerly occurred mainly in children, most patients now are adults with heroin addiction. Of the 39 patients with tetanus treated with meprobamate in the 20 months prior to this writing, 20 were heroin addicts and 19 were nonaddicts. Of these, 14 (70%) addicts and 4 (21%) nonaddicts died (see table). All were adults, except for four children, the youngest being 6 months old, in the nonaddict group. There were no patients with tetanus neonatorum. Because of their debilitation and generally poor nutritional status, heroin addicts with tetanus are very poor risks, responding poorly to all forms of treatment.

Dosage.—Meprobamate was supplied in ampuls containing 400 mg. in 5 cc. of polyethylene glycol. The relative insolubility of the drug in conventional solvents has made it necessary for it to be supplied in this form. The drug must be given intramuscularly, since polyethylene glycol may cause a phlebitis if given intravenously. The dosage employed was 400 mg. every three to four hours for an adult, with relatively less for children. In spite of the fact that 5 cc. is a rather large intramuscular dose, we were surprised to find that it was relatively painless due to the local anesthetic properties of meprobamate.

Results.—Our experience with intramuscularly given meprobamate in the control of tetanus spasms has been so remarkable that we consider the drug to be the most valuable one currently available in the management of tetanus. The specificity of the drug in controlling only those spasms triggered by somatic stimuli has been surprising and somewhat difficult to explain.

Report of Cases

Our first experiences with the use of meprobamate in tetanus were so striking that our first two cases are herewith reported in detail.

CASE 1.—A 30-year-old woman, a known heroin addict, was admitted to Cook County Hospital with stiffness of the back and neck of six hours' duration. Although no objective evidence of tetanus (e. g., nuchal rigidity, trismus, or pathological reflexes) was present, the patient was given 20,000 units of tetanus antitoxin; 1,200,000 units of procaine penicillin G, intramuscularly; and methadone (Dolophine) hydrochloride, 10 mg. intramuscularly every six hours, for control of withdrawal symptoms. Within 12 hours after admission, she developed a stiff neck, increased deep tendon reflexes, abdominal rigidity, and difficulty in opening the mouth. The diagnosis of tetanus was made and the patient transferred to the tetanus service, where a tracheotomy was performed, another 80,000 units of tetanus antitoxin given, and a Levin tube passed. (In narcotic addicts with skin infections, cut-downs for intravenous injections are avoided where possible because of the difficulty in finding veins and the danger of infection.)

Within 24 hours after the onset of the first symptoms, the patient was having generalized spasms. This rapid onset of spasms indicated a grave prognosis. Pentobarbital, 2 grains (125 mg.), and chlorpromazine, 50 mg., were given intramuscularly every four hours. Chlorpromazine was used primarily as a tranquilizer and as a potentiator of barbiturate action.

The patient became rapidly worse, and within 12 hours after onset the seizures were more severe, occurring every few minutes, and management became more difficult. Seizures were precipitated by the slightest noise, by moving the patient, or by attempting to aspirate the tracheotomy tube. It was obvious that a marked increase in dosage of pentobarbital and/or chlorpromazine would be necessary to attain any degree of control of these seizures. Feeling that the patient's rapid course and bad prognosis justified the use of any measures which might offer promise of help, an intramuscular injection of 400 mg. of meprobamate in 5 cc. of polyethylene glycol was administered.

Within 10 minutes dramatic improvement was noted. Not only did the seizures cease but the patient became relaxed; the trismus, as well as the abdominal rigidity and lordosis, disappeared. To our surprise, loud noises or bright lights did not precipitate spasms. We were amazed to find that the patient could be stuck with a pin without precipitating a spasm. This observation was unique in our experience with tetanus, particularly because the patient was not comatose and could respond to simple commands. At this point, an attempt was made to aspirate the tracheotomy tube and the patient had a generalized spasm. Seizures could also be precipitated by gagging the patient with a tongue depressor or by passing a catheter into the bladder. In spite of the fact that somatic stimuli failed to evoke seizures, "spontaneous" spasms were frequently observed. It soon became obvious that these "spontaneous" seizures were associated with evidence of visceral discomfort such as cough, colic, or a plug in the tracheotomy tube. Further observation disclosed that spasms were also precipitated by proprioceptive stimuli from passive movement of a hip or shoulder in turning the patient. In spite of the fact that meprobamate given intramuscularly every three to four hours controlled many of the severe seizures and apparently all of those usually precipitated by noise or other somatic stimuli, the patient's condition continued to deteriorate. Within 48 hours her temperature rose from 100 to 104 F (37.8 to 40.0 C) rectally, her pulse rate increased to 130 per minute and became irregular, and her respiration rate increased to 40 per minute and became irregular and of the Biot type. The patient lapsed into coma and died on the fifth day after admission.

It was of interest to note that while on meprobamate therapy this patient received only 6 to 9 grains (390 to 580 mg.) of pentobarbital every 24 hours as compared to the 18 to 24 grains (1,160 to 1,550 mg.) of this drug usually necessary to sedate other heroin addicts who have tetanus.

Comment.—Our experience with meprobamate in our first patient with tetanus induced us to continue the use of this drug in our next one. Our second patient, who recovered, convinced us that the amazing effect of meprobamate on spasms noted in the first patient was not simply a fortuitous circumstance but represented a remarkable pharmacological effect.

CASE 2.—A 20-year-old man, a nonaddict, had crushed his left thumb in an automobile door nine days before the onset of his first symptoms, which consisted of a mild backache and stiffness of the neck. Within 48 hours he was admitted to the hospital with a full-blown case of tetanus. On admission, he was in acute distress with severe pain in the neck and back, abdominal rigidity, opisthotonus, and generalized spasms every two to three minutes. He was unable to open his mouth more than 0.5 cm. Deep tendon reflexes were hyperactive, and attempts to elicit these responses resulted in convulsive spasms. The temperature was 101 F (38.3 C) rectally, and all over vital signs were normal. Because of the rapid onset of seizures (less than 48 hours after the first symptom) a guarded prognosis was given. A tracheotomy was performed, penicillin therapy started, 80,000 units of tetanus antitoxin administered, the wound débrided, and a Levin tube passed to facilitate feeding. Because of a distended bladder, a retention urethral catheter was inserted.

Since at this time we did not have full confidence that meprobamate alone would effectively control spasms, the patient was first given 3 grains (194 mg.) of pentobarbital and 10 mg. of chlorpromazine intramuscularly; he was then started on therapy with meprobamate, 400 mg. intramuscularly every four hours. This patient did so remarkably well on meprobamate therapy that chlorpromazine was withdrawn and pentobarbital dosage cut to 1.5 grains (97 mg.) intramuscularly occasionally for sleep and control of pain. As in the first patient, within 10 minutes after the injection of meprobamate the spasms ceased entirely. The patient became relaxed and his trismus disappeared; he could now open his mouth to a width of 2.5 cm. He was communicative and responded to commands. Although pinprick, noises, or sudden sprinkling with cold water did not precipitate a seizure, light visceral stimuli such as passing a catheter into the tracheotomy tube did so. In fact endogenous visceral stimuli precipitated "spontaneous" spasms.

Because the patient was conscious and communicative, it was possible to discover some of his visceral complaints and to correct some of them. For instance, when he was having a series of spasms for no apparent somatic reason, he complained of the catheter in his bladder. When asked if he would rather have the nasal or the bladder catheter removed, he vehemently indicated the latter. After this was removed, all of his spasms ceased except hose caused by aspirating the tracheotomy tube or turning him in bed. On another occasion, when began to get spontaneous spasms, the removal of a fecal impaction was followed by their cessation. A distended bladder or intestine would often be associated with spasms.

Even during the most severe period of the illness, spasms were adequately controlled by meprobamate alone with very little pentobarbital. Patients treated previously without meprobamate required as much 18 to 24 grains of pentobarbital in a 24-hour period and, even with this, had only a fair control of spasms; moreover, these patients remained continually stuporous, and the danger of respiratory depression was constantly present. The present patient received a maximum of 6 grains and an average of 3 grains of pentobarbital in any 24-hour period for the first 10 days. Thereafter, his maximal daily dose was only 3 grains with an average of 1.5 grains. At the end of the second [illegible] the tracheotomy tube was removed; at the e[illegible] fifth week the patient was discharged as c[illegible] with some residual stiffness in his muscles.

Comment.—The experience [illegible] in these two cases was repeated and reaffirme[illegible] remaining series of 39 patients. Not only we[illegible]s adequately controlled by meprobamate a[illegible] ven between spasms the patient was more r[illegible] trismus, risus sardonicus, abdominal rig[illegible] arched back disappeared or were markedly le[illegible]. The mouth could be opened wider and the [illegible] could be passively flexed through a much wi[illegible] range.

In practically all instances the onset of drug effectiveness was within 10 to 15 minutes and the duration of effectiveness was 3 to 4 hours. In most patients, complete control of somatically induced seizures was attained by giving 400 mg. of meprobamate in 5 cc. of polyethylene glycol intramuscularly every four hours. By injection, the drug was much more effective than 10 times this dose given orally. It was not possible to contral spasms completely during the acute phase of the disease with as much as 5,600 mg. (14 tablets) of meprobamate in a single orally given dose in two patients in whom this large dose was tried. In convalescent patients or those with relatively mild involvement, however, it was frequently possible to control discomfort and residual local muscle spasm by the oral administration of 800 mg. of meprobamate four times per day. To rule out the possibility that the beneficial effects of the injectable medicament were due to the vehicle, controlled injections of 5 cc. of polyethylene glycol alone were used, without any therapeutic benefit.

In addition to controlling somatically induced spasms, meprobamate had a tranquilizing action which allayed apprehension and made the patient generally more calm and comfortable. Nurs[illegible] greatly simplified. The patients were consci[illegible] communicative, could respond to simple com[illegible] and could make their needs known. It was no[illegible] necessary to insulate the r[illegible] against nois light. Tracheotomy, which had been routinely done in all patients with tetanus, regardless of cause or severity, was now made an elective procedure in the nonaddicts and actually was not done in 6 of the 19 patients in this group.

Effect on Mortality

Since morbidity was so greatly reduced by use of meprobamate, it was of interest to note whether [illegible] not these benefits were reflected in a re[illegible]ced mortality. Our previous experience had in[illegible]cated that drug therapy, even when it controll[illegible] spasms, generally had no effect on mortality. Ei[illegible]teen (46%) of the 39 patients in this series died[illegible] The mortality among the addicts was 70% as [illegible]pared to 21% among the nonaddicts.

The table compares the [illegible]lity in the meprobamate-treated group [illegible] [illegible] that in a previous group treate[illegible] [illegible] other methods. In the 51-month period, [illegible] 1, 1954, to Dec. 1, 1958, there were a total of 90 tetanus patients treated at Cook County Hospital, with 51 deaths, or a mortality of 58%.

Comparative Mo[illegible] in Patients With Tetanus With and out Use of Meprobamate

	Without Meprobamate			With Meprobamate		
	Patients, No.	Died No.	Died %	Patients, No.	Died No.	Died %
[illegible]	36	26	73	20	14	70
[illegible]dicts	15	7	47	19	4	21
[illegible]tal	51	33	65	39	18	46
Onset of Spasms Before 48 Hr.						
Addicts	26	20	80	14	13	93
Nonaddicts	8	5	63	8	3	38
Total	34	25	73	22	16	73
Onset of Spasms After 48 Hr.						
Addicts	4	1	25	6	1	17
Nonaddicts	4	1	25	11	1	9
Total	8	2	25	17	2	12

The treatment of all these patients was similar, except for the drugs used in the control of seizures. All of the patients, except for six in the meprobamate-treated group, were tracheotomized. For the first 31 months of this period, there were 51 patients treated with tribromoethanol (Avertin) and pentobarbital as the main sedative drugs. In 15 of these curarization and artificial respiration had also been used, and in 20 chlorpromazine had also been used. Since there was no appreciable difference in mortality or morbidity in any group in which different treament combinations were used, these are treated as a single group for comparison with the meprobamate-treated group of 39 patients which is the subject of this report.

In the group treated without meprobamate, 65% [illegible]1 patients died as compared to 46% of the [illegible]ents in the meprobamate-treated group—a [illegible] but not remarkable reduction in mortaliy. [illegible] the patients, however, are grouped as addicts [illegible] mortality r[illegible]nained the same—about 70% regardless of type [illegible] treatment used. This is not surprising, since [illegible]ese patients have not only the most severe typ[illegible]f tetanus with rapid onset of seizures and with [illegible]bar involvement but also a considerable degree [illegible] physical and nutritional debility. The cause of death in the heroin addicts with tetanus appears generally not to be tetanus per se but rather some other intercurrent, as yet unidentified, lethal factor. In the nonaddicts with tetanus, however, 7 (47%) of fifteen died before meprobamate was used, and only 4 (21%) of 19 treated with meprobamate died—a reduction in mortality of over 50%.

In order to rule out the possibility that this improvement in mortality in the nonaddict group was fortuitous [illegible] due, perhaps, to the fact that patients with milder cases of tetanus were being treated in the meprobamate series, the group was subdivided into those with a rapid onset of spasms, less than 48 hours, and those with a slower onset, over 48 hours from the appearance of the first symptoms. As previously pointed out, the mortality and severity of tetanus of all types is closely related to the interval between the appearance of the first symptom and the onset of spasms. The shorter this interval of onset, the worse is the prognosis.

From the table it is seen that in addicts with a seizure onset interval under 48 hours, the mortality was always high, from 80% to 93%, regardless of the method of treatment. For the nonaddicts, on the other hand, with onset of spasms less than 48 hours, there was a decrease in mortality from five (63%) of eight in patients not given meprobamate to three (38%) of eight in those on therapy wit meprobamate. Although the number of cases i each of these categories is too small to be o statistical significance, gross inspection indicates trend toward decreasing mortality with meprobamate treatment. The lower mortality in nonaddict as compared to addicts is in part due to the fac that most of the addicts had an onset period of less than 24 hours while most of the nonaddicts in the rapid onset group had onset intervals between 24 and 48 hours.

When the period of onset of seizures is over 48 hours, the mortality is much less (under 25%), regardless of whether the patient is an addict or not. Even in this group with milder cases of tetanus the mortality was less for those on meprobamate therapy (two deaths in 17 patients) than for those who were not given meprobamate (two deaths in 6 patients). It would thus appear that both morbidity and mortality are decreased when tetanus patients are treated with meprobamate, with the exception of heroin addicts with severe tetanus and with rapid onset of seizures.

The fact that the patient treated with meprobamate is more communicative has simplified nursin and has made it possible to discover some of th

What is more difficult to explain, however, is the observation that meprobamate seems to stop only somatically induced spasms, having no effect on those induced by visceral or proprioceptive stimuli (fig. 2C). No information is available as to whether or not meprobamate will protect animals against strychnine seizures evoked by visceral stimulation. In any event, the apparent selective action of meprobamate in preventing only exteroceptively induced tetanus seizures makes one postulate that the site of action of this drug is somewhere in the ascending tracts of the exteroceptive pathways. To our knowledge, no drug has heretofore been found which has such a highly selective action. Experimental studies in animals with strychnine seizures might help to elucidate this rather unique effect.

Some studies in humans, however, have corroborated the selective action of meprobamate on exteroceptive pathways. Nyquist and associates[10] studied the comparative effect of meprobamate, zoxazolamine (Flexin), phenobarbital, and placebos on patients with spinal cord injuries. They found that meprobamate was the most effective drug in relieving spasticity in the skeletal musculature. They were surprised to find, however, that it had relatively little effect on bladder and sphincter musculature in cystometric studies. Although, clinically, in some of their patients a catheter became unnecessary during meprobamate therapy, the effect of the drug on the bladder and vesical neck was equivocal. In other words, these authors also discovered that, whereas meprobamate would decrease spasticity and irradiated responses to somatic stimuli, it apparently had no effect on bladder muscles in response to stimuli elicited from the bladder.

Holliday[11] studied the effect of meprobamate, chlorpromazine, pentobarbital, and a placebo on the disrupting effect of stress on trained performance. The stimuli used in causing the stress were al exteroceptive, and meprobamate was the only d found to have a beneficial effect. The author in not employ proprioceptive or visceral sti ulate their study, but it would be of interest to s proba- as to whether the beneficial effect from visceral mate they observed would be duplicat or proprioceptive stimuli had been u

Summary

Meprobamate, given intram ularly, effectively
controls the spasms of teta evoked by somatic
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treated as a single gr. Meprobamate has
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tracheotomy are concerned. Morbidity has been greatly reduced. Mortality also has been greatly reduced in nonaddicted patients and in addicts with slow onset of spasms (over 48 hours). It has not appreciably reduced the mortality of heroin addicts with tetanus whose spasms generally occur within 24 hours after onset of symptoms, although it has reduced their morbidity and simplified their nursing care. The drug has been found to be safe and harmless and to date is the most effective drug for the control of somatically evoked spasms of tetanus.

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The meprobamate ampuls used in this study were supplied through Dr. Frank Berger, Wallace Laboratories, New Brunswick, N. J., for experimental trial in reducing spasticity and hypertonus in patients with cerebral palsy.

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HYPERURICEMIA—RELATIONSHIP TO HYPERCHOLESTEREMIA AND ACUTE MYOCARDIAL INFARCTION

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and
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Hyperuricemia appears to be a concomitant of myocardial infarction with practically the same degree of frequency as hypercholesteremia. In a group of 35 men studied, 79% manifested serum uric acid levels above 6 mg. per 100 ml. It is recommended that, in assessing the proneness of a person to coronary heart disease, the uric acid level be considered, in addition to the cholesterol or other serum lipid levels, family history, and other factors. It is also advisable to use probenecid prophylactically in such patients.

The high incidence of arteriosclerosis as a complication of gout has been well known for over 50 years,[1] but the question of the more specific relationship of hyperuricemia to coronary artery disease has been raised comparatively recently. Gertler and associates[2] were the first to note a statistically significant incidence of hyperuricemia in a group of patients with coronary heart disease. They reported that, in 92 males who had experienced myocardial infarction prior to the age of 40 years, 24% had serum uric acid levels above 6 mg. per 100 ml. whereas only 6% of a matched control group and 6% of a larger group of unselected controls had a similar degree of hyperuricemia. Actually, hyperuricemia has been defined by some authors as being a level above 5 mg. per 100 ml., and on this basis Gertler and associates found that 48% of the patients with infarct had hyperuricemia, compared with 42% in the matched control group and 31% in the unselected control group.

Although they gave no figures, Dreyfuss and Czaczkes[3] mentioned that the incidence of hyperuricemia in their group of patients with coronary disease was "by no means negligible."

The present study was undertaken to further clarify the apparent association between hyperuricemia and coronary artery disease, as well as that between these two entities and hypercholesteremia. Basically the method utilized by us consisted of determining the serum uric acid and cholesterol levels in a relatively unselected group of patients admitted consecutively to a general hospital with a verified diagnosis of acute myocardial infarction. No control group was included in this study, inasmuch as we felt that it is practically impossible to determine the presence or absence or degree of coronary atherosclerosis in any given person prior to the appearance of overt coronary disease as manifested by myocardial infarction or by recognizable angina pectoris.

Methods

Fifty consecutive patients admitted to the Mt. Sinai Hospital, Cleveland, with a verified diagnosis of acute myocardial infarction were selected for study. Patients above 70 years of age were rejected from this series because of the frequent association of complications, debility, and other diseases. Diabetic patients were likewise omitted because of hypercholesteremia attributable to the diabetic state per se. In addition, all patients who died less than 48 hours after admission were also excluded.

The diagnosis of myocardial infarction in all cases was confirmed by the typical electrocardiographic changes, as well as by elevated serum glutamic oxalacetic transaminase levels. Serum uric acid and cholesterol levels were determined in each patient shortly after admission and in most patients and subsequent intervals during the course of their hospitalization.

The uric acid level was determined by the phosphotungstate–sodium cyanide method of Brown. The standard method of Bloor was used for determination of the serum cholesterol level.

Results

Tables 1 and 2 summarize the pertinent data in 35 male and 15 female patients. The order of listing and numbering of the patients has been arbitrarily arranged according to age, rather than by date of admission. In the male group 5 were between 31 and 39 years of age, 7 were between 40 and 49, 8 were between 50 and 59, and 15 were between 60 and 69. The youngest female study was 49 years of age, and an equal were in the sixth and se of the patients

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From the Division of Medicine, Mt. Sinai Hospital.

levels over 5 mg. per 100 ml. In the group with uric acid levels above 6 mg. per 100 ml., 15 of the 19 patients under 60 years of age were in this definitely hyperuricemic category. The three males in our series who had normal uric acid levels were all over 60 years of age. The average serum uric acid level of the entire group of males was 6.5 mg. per 100 ml., and the average value in those below the age of 60 years was 7.2 mg. per 100 ml.

Table 1.—*Serum Uric Acid and Cholesterol Levels in Thirty-five Men with Myocardial Infarction*

Case No.	Age, Yr.	Cholesterol, Mg. %		Av. Uric Acid, Mg. %
		Admission	Av.	
1	31	380	360	7.7
2	36	240	240	5.8
3	38	300	309	6.2
4	38	210	203	5.4
5	38	352	442	9.4
6	41	315	330	6.1
7	42	350	368	7.7
8	42	290	...	8.8
9	44	362	356	8.1
10	46	284	290	7.0
11	46	324	...	7.4
12	49	332	336	5.9
13	50	346	332	5.5
14	51	318	...	6.2
15	51	230	...	8.7
16	52	285	...	6.4
17	54	316	...	8.1
18	54	374	...	8.6
19	57	320	...	7.0
20*	59	280	260	5.1
21	60	390	425	6.9
22	61	228	...	4.6
23	61	392	371	7.3
24	62	338	341	4.6
25	62	300	...	4.2
26	64	300	...	5.7
27	64	350	300	5.4
28	65	253	...	5.0
29	65	184	186	5.8
30	65	296	...	6.9
31	65	300	230	5.6
32	67	244	237	5.5
33	68	1,282	...	5.6
34	69	301	...	6.5
35	69	292	...	6.4

* Gout also present, treated with probenecid (Benemid).

In 15 female patients the average uric acid level was 5.3 mg. per 100 ml. Six had levels above 6 mg. per 100 ml. and another four had levels between 5.0 and 5.9 mg. Thus, 10 of the 15 female patients had uric acid levels in excess of 5 mg. per 100 ml.

Of the 35 males only 5 had serum cholesterol levels below 250 mg. per 100 ml., and only 2 of the
15 femal used, d a serum cholesterol level below 250
used. Sinc of the patients who had serum
mortality or rminations subsequent to ad-
ent treament 10 mg. per 100 ml.
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mari In the group treat the pati tients, it is
barbiturate act l patients di proce nd one fe-
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but not rem

Comment

There is relatively wide acceptance today of the concept of the relationship between hypercholesteremia and coronary heart disease, and increasing numbers of students of the subject are willing to assign a pathogenic role to this lipid in the development of coronary artery sclerosis. One reason for considering cholesterol as an etiological agent is the almost universal finding of elevated serum cholesterol levels in patients with proved coronary artery disease. In a study of nearly 5,000 healthy men 40 to 59 years of age, over a period of two years 32 developed myocardial infarction and 86% of these had had excessively high cholesterol levels at the beginning of the study.[4]

Our results also amply illustrate the almost necessary correlation between elevated serum cholesterol levels and coronary artery disease; in our series 43 of the 50 patients had levels above 250 mg. per 100 ml. It was our impression that the stress incident to the acute myocardial infarction itself plus the emotional trauma produced by admission to a hospital caused relatively little if any further increase in cholesterol levels, for we found that in one-half the cases the admission cholesterol level was not higher than that in subsequent determinations. The logical consequences of this apparent but as yet not wholly proved role of hypercholesteremia in the development of coronary artery disease are (1) the use of the cholesterol level in predicting proneness to coronary disease and (2) the attempt to prevent premature development and/or further progress of coronary atherosclerosis by reducing serum cholesterol levels by means of dietary management and drugs.

Table 2.—*Serum Uric Acid and Cholesterol Levels in Fifteen Women with Myocardial Infarction*

Case No.	Age, Yr.	Cholesterol, Mg. %		Av. Uric Acid, Mg. %
		Admission	Av.	
36	49	200	205	6.2
37	50	300	...	6.5
38	52	268	...	6.4
39	53	430	400	4.2
40	55	356	382	5.1
41	55	280	260	3.8
42	57	466	...	6.9
43	58	310	...	5.7
44	61	420	...	4.9
45	65	418	...	5.7
46	65	292	...	5.0
47	67	290	...	3.4
48	67	216	250	3.1
49	68	280	...	6.0
50	70	336	280	7.6

As found in our study, hyperuricemia also appe
to be a concomitant of myocardial infarction
practically the same degree of frequency as h
cholesteremia. In our series, in the group
below the age of 60—the so-called premat
nary group—this fact was particularly s
% of these patients manifested ser

levels over 6 mg. per 100 ml. Further emphasizing the significance of this finding is the fact that in reports of groups with neither gout nor coronary disease those patients with serum uric acid levels above 6 mg. per 100 ml. comprised only from 3 to 17% of the total.[5]

Although at present this relationship is not widely appreciated, at least one other group of investigators is impressed with the potential significance of hyperuricemia in the coronary problem. Gertler and associates [2] have incorporated the uric acid level in their so-called CUP ratio: K equals cholesterol level (mg.%) multiplied by uric acid level (mg.%) and divided by phospholipid level (mg%). This is used in assessing the proneness to coronary heart disease of a given person, and, thus, these workers recognize that the higher the uric acid level, just as the higher the serum cholesterol level, the greater is the probability that coronary artery disease will eventuate.

Although our results clearly demonstrate the extremely frequent coexistence of hyperuricemia and coronary artery disease, the explanation for this association is not obvious. It is known that hyperuricemia is inherited as a simple Mendelian dominant characteristic,[6] as is hypercholesteremia.[7] Heredity or genetic predisposition has been considered to be a most significant factor in the development of coronary artery disease itself.[8] One might then speculate as to the genetic linkage of these three traits, i.e., hyperuricemia, hypercholesteremia, and coronary disease. In this connection it is noteworthy that, whereas Gertler and associates [2] found that 48% of their patients with myocardial infarction had hyperuricemia, in our series almost twice as high an incidence was found. One feature of our series that is presumably somewhat different is the high percentage of Jewish patients in our hospital. Inasmuch as this group is extremely inbred, it would appear that a hereditary defect, such as hyperuricemia and, for that matter, hypercholesteremia, would tend to be disproportionately high in incidence.

Regardless of the explanation for the association of hyperuricemia and coronary artery disease, the predictive value of this parameter seems apparent. Of greater importance is the question of what part, if any, uric acid plays in the pathogenesis of coronary atherosclerosis. Here again little is known of the role played by uric acid in the development of vascular disease. Traut and co-workers [9] demon-
ated deposits of urate crystals in the proliferated
ma of arteries or in organized thrombi, and this,
urse, represents one mechanism by which uric
may participate in the process of vascular
tion. Another possible factor is that uric
surface-active agent and may facilitate
n of lipids in the subintimal tissues of
vessels.

It would appear that more investigative work along these lines is indicated for the elucidation of the role of uric acid in coronary artery disease. This is particularly important since there is already available a most satisfactory uricosuric agent for the control of elevated serum uric acid levels, namely, probenecid. We feel that consideration should be given to the possible benefits to be derived from the administration of this drug to patients with hyperuricemia, even in the absence of clinical gout. This particularly applies to those patients who also have elevated cholesterol levels and family histories of coronary artery disease, for if it should ultimately be established that elevated serum uric acid levels promote and facilitate the development of coronary atherosclerosis, a certain amount of "protection" may thereby be afforded. Along these lines, mention should be made of the uricosuric action of the coumarin compounds, inasmuch as the possible benefits of anticoagulant therapy with these agents, in both short-term and long-term therapy, on coronary artery disease ha been ascribed by some investigators to the reduction in serum uric acid levels produced by thes drugs.[10]

Summary

Serum uric acid and cholesterol level determin
tions were made on 50 consecutive patients wit
acute myocardial infarction, including 35 men ar
15 women. Twenty of the men and six of the wome
had serum uric acid levels above 6 mg.%
men and 10 women had levels a
Forty-three of the 50 patients had serum cholester
levels above 250 mg.%. Only one man and o
woman had normal levels of both uric acid a
cholesterol.

Because of the high incidence of hyperuricem
in association with myocardial infarction, it is r
ommended that the uric acid level be conside
in assessing the proneness of a person to coron
heart disease, along with the cholesterol or ot
serum lipid levels, family history, and other fact
It is also advisable to use probenecid prophy
tically in persons with hyperuricemia, particul
in those with hypercholesteremia and genetic
stitutions indicating proneness to coronary h
disease.

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HEMOGLOBINURIA AFTER MASSIVE INTRAPERITONEAL HEMORRHAGE

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Determination of plasma hemoglobin levels may be a useful clinical tool for detection of bloody serous effusions when direct aspiration cannot be carried out successfully. After such extravasation, there is usually rapid absorption of unchanged blood cells through the diaphragmatic peritoneum, with return to the general circulation through mediastinal and parasternal lymphatics. Any delay in this absorption process would probably increase the degree of hemolysis. In this patient, massive hemolysis occurred. Factors probably responsible included excessive load on the lymphatic system, extreme abdominal distention, and pulmonary edema causing engorgement of the right lymphatic duct, with delayed appearance of hemoglobinemia and hemoglobinuria.

he appearance of free hemoglobin in the plasma urine after intraperitoneal hemorrhage is a henomenon which has not received much attenion in recent medical literature, although its use diagnostic sign was described over 20 years go. 28

The following case of massive hemoglobinuria is eported because it reemphasizes the need for wareness that red blood cells and hemoglobin can e absorbed intact through serosal surfaces.

Report of a Case

A 31-year-old woman was transferred to Beth rael Hospital, Boston, on Feb. 9, 1958, for evaluaon of persistent blood loss postoperatively. The tient had a history of nine pregnancies, the first o resulting in normal full-term spontaneous deries but the remaining seven ending prematurefive because of spontaneous abortions in the rth to fifth month of gestation and two with arean sections in the sixth month for stillborn uses. There was no history of bleeding tendency of anemia, and she had otherwise been in good lth.

n Jan. 29, 1958, 11 days prior to her transfer to Beth Israel Hospital, a four-and-one-halfth pregnancy terminated in spontaneous abor. The placenta was retained, and the next day as removed by dilation and curettage at another hospital. She was well until Feb. 7, two days prior to transfer, when vaginal hemorrhage suddenly occurred. She was readmitted to the other hospital in shock, with pulse rapid and thready and blood pressure unobtainable. Examination revealed retained placental fragments. Because uterine packing was unsuccessful in stopping the flow of blood, a supracervical hysterectomy was performed with the patient under general anesthesia. The surgeons

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ice, Beth Israel Hospital, and the Department mari School. Dr. Cohn is now Senior Assistant barbiturvice Hospital, Galveston, Texas.

noted that the uterine attachments were friable, particularly on the right side where more sutures than usual were required to establish hemostasis.

Two units (1,000 cc.) of whole citrated blood was given before and during operation, and blood pressure was maintained at 120/80 mm. Hg. Estimated blood loss during the operation was 500 cc. Postoperatively she again went into shock, and over the course of the next 48 hours she received intravenously 8 more units of whole blood in addition to levarterenol, 1,000 cc. of isotonic sodium chloride solution, 2,000 cc. of sodium lactate solution, 3,000 cc. of dextrose and water, 2 Gm. of tetracycline, and 300 mg. of hydrocortisone. Despite the 10 units of blood, her hematocrit value stayed below the admission level of 30%. There was no sign of external bleeding; the wound remained clean; and no abdominal fluid wave was demonstrable. Eight units of blood used in transfusion had been compatible, A positive, while 2 units had been A negative.

Laboratory Findings in Patient with Hemoglobinuria

	Hospital Day																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Hemoglobin level, Gm. per 100 ml. ...	10.0	10.0	10.8	12.5	13.3	14.1	13.3	13.3	12.5	11.2	10.8	11.5	12.5	11.5	11.2	11.2	11.2	10.8	11.0	10.8	12.2	10.1	11.5
Hematocrit value, %	30				37	39	40	40	39	33	35	34	36	34	35		37	34	31	32		32	33
Reticulocyte count, %				7.9	8.2	7.0	6.4		1.4	3.1	2.5	3.0	1.4	2.0	2.5	3.2	3.2	5.2	3.1	3.9	2.8	1.8	5.0
Serum hemoglobin level, mg. per 100 ml.				+	++ +	633	++ +	++	81	++	++	+	45										
Urine hemoglobin ..				++	++ ++	++ ++	++ ++	++ ++	++ +	0	0	0	0										
Serum bilirubin level, mg. per 100 ml. ...				2.2	3.8	2.8			4.1	2.5			1.3										

On the second postoperative day tachypnea and facial edema were noted. Her hematocrit value was 30% and hemoglobin level 70%. She was transferred to the Beth Israel Hospital for further study. On admission she was pale and cyanotic and had marked tachypnea. The temperature was 99 F (37.2 C) rectally, the pulse rate 120 per minute and regular, the respiratory rate 48 per minute, and the blood pressure 110/60 mm. Hg. The neck veins were markedly distended and pulsating above the angle of the jaw. There were dulness and absent breath sounds at the base of the right lung, but the lungs were otherwise clear to auscultation. The left border of cardiac dulness was percussed at the midclavicular line in the fifth interspace. No murmurs were heard. The abdomen was distended, with dulness in the flanks, slight shifting dulness, but no definite fluid wave. The intestinal sounds were diminished. The suprapubic operative incision was healing normally. There were no ecchymotic areas and no evidence of bleeding diathesis. The skin was sallow but not icteric.

Urine findings were within normal limits. Examination of the blood revealed a hemoglobin level of 10 Gm. per 100 ml., hematocrit value 30%, and white blood cell count 12,000 per cubic millimeter, with 85% neutrophils. The clotting time, platelet count, fibrinogen titer, osmotic fragility test result, and Coombs' test result were all within normal limits. The serum sodium level was 141 mEq. per liter, potassium 3.0, chloride 103, and carbon dioxide 35. Prothrombin content was 65%, and prothrombin consumption was normal. Result of an Aschheim-Zondek test was negative. Stools were negative for occult blood. Cultures of the urine and blood were negative. A chest x-ray on admission showed findings consistent with massive pulmonary edema and a right pleural effusion. Roentgenogram of the abdomen revealed air in the small intestine consistent with an ileus. An electrocardiogram showed T-wave changes consistent with hypokalemia.

Because of the admission impression of possible intraperitoneal hemorrhage, a diagnostic abdominal tap was performed in the right lower quadrant. However, no free fluid or blood was obtained. The pulmonary edema was thought to be due to hypervolemia from circulatory overloading with sodium-containing fluids and steroids during the postoperative period. She was treated with a low-sodium diet and mercurial diuretics. On the third hospital day, because of persistent respiratory distress, bilateral thoracenteses were performed, yielding 400 cc. on the right and 40 cc. on the left of grossly bloody fluid. By the next day venous distention had disappeared and the lungs had cleared.

On the fourth hospital day her urine was noted to be red and her serum darkly colored. The serum bilirubin level was 2.2 mg. per 100 ml., and the blood hemoglobin level, which had been stable, showed a precipitous increase from 10.8 to 12.5 Gm. per 100 ml. A reticulocyte count was 7.9% (see table). Spectroscopic examination of the serum showed the absorption bands typical of oxyhemoglobin and methemalbumin. Results of repeat Coombs' test, indirect Coombs' test against minor antigens, and tests for hemolysis in cold or acid were all negative. Repeat right thoracentesis yielded 20 cc. of grossly hemolyzed blood. Abdominal paracentesis in the left lower quadrant was productive of a small amount of gross blood with a hematocrit value of 13%. Spectroscopic examination of the plasma from this specimen showed the bands of oxyhemoglobin only. Quantitative hemoglobin determination on this plasma by the benzidine method of Bing and Baker (cited by Ham[2]) was 1,240 mg. per 100 ml. (normal plasma contains less than 5 mg. per 100 ml. by this method).

Massive hemoglobinuria with black urine persisted for six days. Significant elevation of the plasma hemoglobin level was detected for 10 days and probably persisted for much longer. A maximum plasma concentration of 633 mg. per 100 ml. was observed on the 6th hospital day, and a level of 45 mg. per 100 ml. was still present on the 13th day, the last day on which quantitative determinations were done.

Throughout the first three weeks of hospitalization, the patient persistently had a temperature of up to 102 F (38.8 C) and moderate abdominal distention. A mass gradually became prominent in the right lower quadrant, and x-rays of the abdomen showed evidence of incomplete obstruction of the small intestine. However, she was able to take food orally and had regular bowel movements. The mass became palpable rectally, and on the 18th hospital day culdotomy was performed with the hope of evacuating it vaginally. Aspiration, however, produced only 10 cc. of hemolyzed, dark brown blood which was sterile on culture. Because it was felt that loculation of the blood had occurred, no further attempts at evacuation were made.

Over the course of the next week her temperature returned to normal, her appetite improved, she gained weight, the abdominal mass became smaller, and her hemoglobin level remained stable. She was discharged on the 28th hospital day to complete her convalescence at home.

Comment

The complete absorption of intact red blood cells placed in the peritoneal cavity has been repeatedly demonstrated by clinical observations as well as by experimental studies. Donor blood injected intraperitoneally in animals may disappear entirely within 24 hours, and elevations of the red blood cell count and hemoglobin concentrations in the circulating blood may be detected almost immediately.[3] Intraperitoneal transfusions of oxalated blood have been used in infants with satisfactory results.[4]

Studies with use of labeled red blood cells in animals[5] and human subjects[6] have demonstrated that absorption of intraperitoneal blood begins immediately; however, up to two weeks may be required for complete incorporation of this blood into the circulation. Absorbed red blood cells have a normal life span.[6b]

The mechanism of absorption from the serous cavities has been reviewed by Courtice and Simmonds.[7] Protein and cells are absorbed from the peritoneal cavity almost exclusively through the diaphragmatic peritoneum, passing into the circulation by way of the mediastinal and parasternal lymphatics, most of which empty into the right lymphatic duct. Absorption from the pleural cavity takes place through the lower mediastinal pleura and costal parietal pleura. The protein and cells then pass through the same lymphatic channels to drain into the right lymphatic duct. The discrepancy noted in the literature between the rapidity of disappearance of blood from the peritoneal cavity and the delay before all of it can be accounted for in the circulation may be due in part to the slow passage through the parasternal and mediastinal lymphatics.[6a] Indeed, Courtice and Simmonds[7] noted in animal studies that blood was occasionally extravasated into the pleural cavity from engorged parasternal lymphatics. This mechanism could explain the bloody pleural effusion found in the case reported here.

The amount of intraperitoneal blood which is hemolyzed prior to its absorption has not been well quantitated. Courtice and co-workers[8] studied the peritoneal reaction which follows the introduction of blood and noted that only a small percentage of the macrophages contained phagocytosed red blood cells. Although lymph nodes in the absorptive pathway did contain large numbers of macrophages engorged with red blood cells, these authors concluded that the actual number of cells lysed was extremely small in comparison to the number absorbed intact. However, apparently enough hemolysis may occur to produce detectable hemoglobinemia or hemoglobinuria from absorption of free hemoglobin. Two of the dogs studied by Hahn and associates[5] were noted to develop hemoglobinemia or gross hemoglobinuria after the introduction of blood into the peritoneal cavity. Pommerenke[1b] described three cases of ruptured ectopic pregnancies in patients in whom hemoglobinuria was demonstrable either grossly or spectroscopically.

Any delay in the usually rapid absorption after hemorrhage into a serous cavity would probably increase the degree of hemolysis by allowing more time for the macrophage system to lyse the cells prior to their return to the circulation. Blood which clots in a serous cavity is no longer absorbable as cellular elements and must be absorbed as hemoglobin and bile pigments. Pritchard and Adams[6b] placed radioactive chromium-labeled clottable blood and small clots into the peritoneal cavities of patients undergoing laparotomy and noted much less absorption than when citrated blood was introduced. They made no observation for hemoglobinuria or hemoglobinemia. Whereas small amounts of blood may be easily handled by the lymphatic system, in massive hemorrhage the lymphatics could become engorged, thus delaying the complete emptying of the serous cavity and probably increasing the amount of hemolysis. In addition, normal diaphragmatic movement plays an important part in peritoneal and pleural absorption by speeding lymphatic drainage and flow.[9] The presence of abdominal distention, ileus, and general inactivity which frequently accompany conditions associated with hemorrhage into a serous cavity would all tend to diminish diaphragmatic movement and further delay absorption.

In the patient presented in this report massive hemolysis did occur. Although it is possible that the blood was initially hemolyzed retroperitoneally and later ruptured into the peritoneal cavity, it is consistent with known physiological mechanisms to postulate that the unusual amount of hemolysis occurred within the peritoneum. The amount of clottable intraperitoneal blood, estimated to be about 3,500 cc. on the basis of transfusion requirements, was approximately equal to this woman's total blood volume. This quantity undoubtedly exceeded the absorptive capacity of the lymphatic system. The patient suffered from extreme abdominal distention, ileus, and partial intestinal obstruction during her hospitalization, thus further delaying the absorptive process. In addition, she had pulmonary edema during the first three hospital days. Pulmonary edema fluid is reabsorbed in large part by way of the lymphatics with ultimate drainage into the right lymphatic duct,[7] the same channel by which intraperitoneal and intrapleural blood returns to the circulation. The pulmonary edema fluid may have engorged the right lymphatic duct, further slowing the drainage from the peritoneal cavity and perhaps accounting for the delay in appearance of hemoglobinemia until the fourth hospital day.

Nonsurgical management of such a large collection of intraperitoneal blood is undoubtedly rare. However, small to moderate collections of bloody fluid in the pleural or peritoneal cavities are encountered in a wide variety of clinical situations. Some hemolysis must occur in all these bloody serous effusions, and the paucity of observations of hemoglobinemia and/or hemoglobinuria in these conditions may be due to a lack of awareness of the occurrence of this phenomenon. The presence in the circulation of the hemoglobin released by the lysis of only 5 cc. of blood would raise circulating plasma hemoglobin values to almost five times the normal value, a quantity easily recognizable by a simple colorimetric methods.[2] It is, therefore, suggested that determination of plasma hemoglobin levels may be a useful clinical tool for the detection of bloody serous effusions when direct aspiration cannot be carried out.

Summary

A case of massive hemoglobinuria occurred after postoperative intraperitoneal hemorrhage. Many physiological mechanisms may contribute to hemolysis of blood in a serous cavity. The determination of plasma hemoglobin levels may be used as a tool in the detection of intraperitoneal or intrapleural blood.

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THERAPEUTIC IMPORTANCE OF ISONIAZID—The antituberculous effect of isoniazid is so great that its use is indicated in every case in which susceptible tubercle bacilli are found. In the absence of gross caseation and destruction the inclusion of other drugs adds little to the results achievable. In the presence of pulmonary cavitation, the therapeutic effect of isoniazid is enhanced about equally by daily streptomycin or PAS.—E. Rothstein, The Eighteenth Veterans Administration—Armed Forces Conference on the Chemotherapy of Tuberculosis, *The New England Journal of Medicine,* June 25, 1959.

PHENTOLAMINE HYDROCHLORIDE IN PREVENTION OF CUTANEOUS NECROSIS DUE TO LEVARTERENOL

A. Stephen Close, M.D., Wood, Wis.

> *It is reasonable to assume that the mechanism by which phentolamine reverses the ischemia associated with extravasation or tissue diffusion of levarterenol is through blockage of action by the latter on adrenergic effector cells. Accumulated evidence indicates that cutaneous necrosis is a preventable complication of levarterenol administration if careful observation for ischemic areas is carried out in all patients who have received levarterenol, with prompt institution of prophylactic instillation of phentolamine when indicated.*

Levarterenol (*l*-norepinephrine) (Levophed) bitartrate is a potent vasopressor agent. It is the specific active substance released at adrenergic nerve endings. The clinical indications for its use have included the hypotension associated with myocardial infarction, toxemia, sepsis, surgical removal of pheochromocytomas and sympathetic chains, and overdosage of adrenolytic agents. Its value in the treatment of hypotension associated with hypovolemia is questionable.

Cutaneous necrosis has been a serious complication of the intravenous use of levarterenol as evidenced by publication of reports of this complication in 61 patients during the period ending July, 1956.[1] The ultimate cause of the necrosis is prolonged ischemia of the skin and subcutaneous tissue due to marked constriction of the vessels supplying these tissues. The necrosis can readily develop when extravasation of levarterenol occurs. However, sloughs are common when extravasation is prevented by ligation of the vein containing a cannula. In this instance marked spasm of the vein and its vasa vasorum appears to be followed by diffusion of levarterenol into adjacent tissues. On the basis of experimental work in animals, three separate investigators[2] have recommended very similar methods for preventing this complication by local administration of phentolamine (Regitine) hydrochloride into ischemic tissues. This report is an analysis of the results of clinical use of one of these experimental methods during a three-year period at the Wood (Wis.) Veterans Administration Hospital.

Method

At the beginning of the study period all physicians and nurses in the hospital were apprised of the possibility of cutaneous slough occurring as a complication of administration of levarterenol. They were informed that according to laboratory experience, areas of ischemia are always present for at least four to six hours before irreversible skin changes occur and that these areas are obvious if one periodically examines the extremity for areas of pallor, decreased skin temperature, and tenderness along the course of the infusion vein.

Whether resulting from extravasation or diffusion, ischemic areas were infiltrated thoroughly subcutaneously with 5 to 10 ml. of saline solution containing 2.5 mg. of phentolamine and 300 units of hyaluronidase. For ischemic areas larger than approximately 30 sq. cm., one-half of the area was so infiltrated and the remaining half similarly infiltrated 30 minutes later. This practice was followed in order to avoid giving more than 2.5 mg. of phentolamine in one dose, although in no instance was there any detectable change in pulse or blood pressure after use of the phentolamine in the manner described.

After treatment of an ischemic area, the levarterenol administration was continued through the same vein unless, or until, an area of ischemia appeared for a second time. If this occurred the area was treated with the phentolamine mixture, and the levarterenol was subsequently administered through a cannula fed into an iliac vein through a high saphenous phlebotomy opening.

Physicians were requested to fill out a data sheet each time an area of ischemia was treated. This sheet requested information regarding the appearance of ischemic areas before and after treatment, an estimate of the duration of ischemia, and the eventual outcome of the treated area.

Results

Prior to the study period sloughs due to levarterenol occurred at the rate of from two to three per year at our hospital. Only one slough occurred in the three-year study period; this slough occurred in a patient whose extremity was not inspected periodically, and a large black gangrenous area of skin was present before prophylactic therapy could be instituted.

The phentolamine infiltration was used 26 times in 20 patients, and in no instance was there any observable systemic manifestation conceivably due to the phentolamine, and in no patient so treated did slough occur.

Clinical Investigator, Veterans Administration Center.

As indicated in the table, coldness and pallor were consistent signs of ischemia, the former being noted in 92% and the latter in 100% of the patients. Pain and edema were noted in approximately half the patients with significant pallor. Purple and white mottled discoloration was noted in five patients, and bleb formation was noted in these same five. Development of a slough appeared almost certain in these five patients prior to prophylaxis with phentolamine.

The average estimated duration of administration of levarterenol prior to the development of ischemia in these cases was 16 hours. In four cases ischemia appeared within two or three hours after administration of levarterenol was started. The duration of ischemia was roughly estimated when possible (utilizing observations made by patients and nurses, primarily) and averaged two and one-half hours, with a range of from one to five hours. Ischemia was not noted in any of the instances of administration of levarterenol directly into the iliac vein where a large flow is present.

Symptoms and Signs Noted in Patients with Impending Sloughs

	Patients	
	No.	%
Coldness	24	92
Pallor	26	100
Pain	15	58
Bleb formation	5	19
Mottled purple and white discoloration	5	19
Edema	13	50

Comment

Experimental evidence has indicated that phentolamine blocks levarterenol action on adrenergic effector cells. It is reasonable to assume that this is the mechanism by which phentolamine reverses the ischemia associated with extravasation or diffusion of levarterenol. It was effective in all instances in this series when given before development of obvious necrosis. Undoubtedly a contributing factor in the decreasing incidence of sloughs, however, is the increasing awareness of the problem on the part of physicians and nurses and the periodic inspection of extremities of patients to whom levarterenol is being administered. Tolazoline (Priscoline) hydrochloride has been successful in prevention of sloughs experimentally, but its relief of ischemia is slower and a much larger does appears to be necessary.[2a] Piperoxan hydrochloride has also been recommended after trial in four cases,[3] and on the basis of its pharmacological properties one could predict its clinical effectiveness. Both histamine and methacholine (Mecholyl) bromide iontophoresis have been used successfully,[4] but these would seem somewhat cumbersome methods in comparison with the other methods described.

Summary

The accumulated evidence indicates that cutaneous necrosis is a preventable complication of administration of levarterenol (*l*-norepinephrine) (Levophed) bitartrate. Careful observation of patients receiving the drug plus prompt institution of prophylactic infiltration with phentolamine has been completely successful in preventing sloughs during a three-year period.

Veterans Administration Center, West National Avenue at 54th Street (14).

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PENICILLINASE FOR REACTIONS TO PENICILLIN.—Once a full-blown penicillin reaction occurs the drug of choice is penicillinase. This enzyme is not only dramatically life-saving in such an emergency but also it rapidly ameliorates the severe symptoms associated with the penicillin reaction. . . . One must remember that while the remarkable benefits of penicillinase are due to its capacity to completely inactivate penicillin as an allergen, it also destroys its therapeutic or antibiotic powers. Therefore, other antibotics or chemotherapeutic agents must obviously be employed if the clinical indications of infection still warrant such alternative therapy.—F. F. Yonkman, M. D., New Drugs for Old Uses and New Uses for Old Drugs, *The Journal of the Michigan State Medical Society,* June, 1959.

CLINICAL NOTES

CAROTID ARTERY THROMBOSIS IN PERSONS FIFTEEN YEARS OF AGE OR YOUNGER

Robert G. Fisher, M.D.
and
Karl R. Friedmann, M.D., Hanover, N. H.

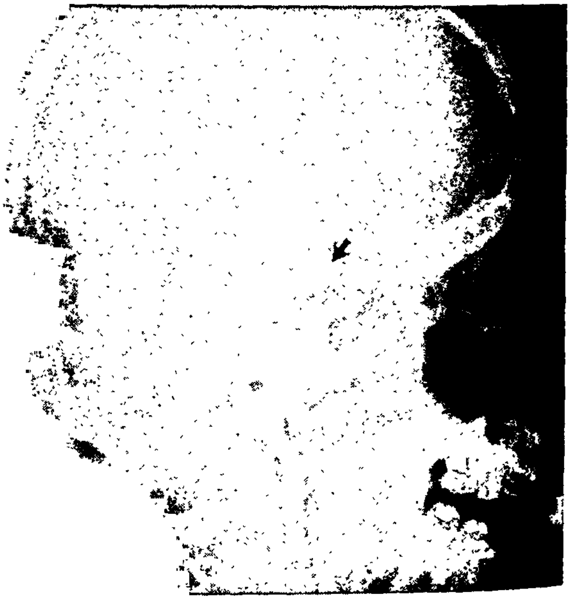
Thrombosis of the internal carotid artery is a major factor in the sudden occurrence of hemiplegia in patients 45 years of age or older. This entity may occur in persons 15 years of age or younger. Our experience with the following recent case has prompted a review of the literature.

Report of a Case

A 15-year-old high-school football player was admitted in a semiconscious condition with marked hemiparesis on the left. He had been in excellent health except for a mild headache prior to "warming up" on the football field. He suddenly fell to the ground unconscious and had a convulsion. He was taken to the office of a nearby physician and sent to the Mary Hitchcock Memorial Hospital. On examination he was drowsy, confused, and incontinent but not aphasic. There were no bruises about his scalp. His pulse was 60 beats per minute, but other vital signs were normal. A marked weakness of the face, arm, and leg was present on the left side, with an extensor plantar response. The abdominal reflexes were absent on the left. The carotid pulses in the neck were normal. On examination, the heart, lungs, and abdomen were normal. X-rays of the skull disclosed a questionable fracture in the right temporal region. Bur holes were made bilaterally to rule out an epidural hemorrhage; no abnormality was found. Bilateral carotid and vertebral arteriograms revealed a thrombosis of the right internal carotid artery just beyond the origin of the posterior communicating artery. Because of progression of the hemiparesis, anticoagulant therapy, as well as massage and passive exercises, was started. The patient was belligerent and disturbed throughout the first 10 days of his illness. The anticoagulant therapy was discontinued after two weeks, since his hemiparesis had not improved. However, a week later function began to return, so that 15 months after the onset of his illness he could walk with a spastic left leg. His left arm is useless. He has returned to school and is doing satisfactorily, although his work is reduced in both quality and quantity. There is no facial weakness.

Comment

We have found 16 cases reported in the literature of internal carotid artery thrombosis occurring in persons 15 years of age or younger. Since the majority of reports deal with the older age groups, one gains the impression that most cases are caused by arteriosclerotic changes in the vessel wall, which cause progressive narrowing of the lumen and thus predispose to thrombosis of the vessel. However, the factor of trauma has always been questioned in these cases—whether it be direct or indirect to the region of the neck. In the case we are reporting, one wonders if there may have been some injury to the carotid artery at the time the patient was "warming up" to play football.



Anteriogram showing thrombosis of right internal carotid artery.

From Mary Hitchcock Memorial Hospital.

In reviewing the cases of this study, no follow-up statements were available in 4 of the 16 cases. One patient died, and 11 were improved in their neurological status. Six of these 11 returned to normal. The sex was reported in 11 of the cases; it is of interest that 9 of these were males. No operations were performed on the artery. It is also of interest that one patient died after an initial episode at the age of 7 years.

Summary

A case of internal carotid artery thrombosis occurred in a 15-year-old boy. A survey of the literature indicates 16 other cases in children aged 15 years or younger. Of the 17 patients, only 6 are known to have returned to a normal neurological status.

Addendum

Since the submission of this report Stevens (*Pediatrics* 23:699, 1959) has published a report on three cases of carotid artery thrombosis, in girls aged 5½, 13, and 1. The first two cases are included in the table; only the one-year-old, who had endocardial fibroelastosis, has not been reported on previously. In this case the occlusion was at the siphon and the infant died two and one-half months after the onset of symptoms.

Summary of Reported Cases of Internal Carotid Artery Thrombosis in Persons Fifteen Years of Age or Younger

Author	Age, Yr.	Sex	History and Findings	Site of Occlusion	Treatment and Remarks
King, A. B., and Langworthy, O. R.: Arch. Neurol. & Psychiat. 46:835, 1941	7	M	Pneumonia 6 mo. before. Fell unconscious; awoke with hemiplegia on left. Blind right eye with white disk. Pupil larger. Spastic left-sided weakness	No angiogram	No specific treatment. Gradual improvement. Could walk unaided in 6 mo.
Krayenbuhl, H., and Weber, G.: Helvet. med. acta 11:289, 1944	15	F	Paralysis on left side at age 13. Recurrence 2 yr. later. Left-sided paralysis	1 cm. above origin	Vessel examined, but no follow-up available
Moniz, E.: Med. contemp. 65:111, 1947	14	M	Jacksonian attacks on right monthly since age 9. Weakness of right hand	At origin	Not stated
Riechert, T.: Nervenarzt 11:290, 1938	13	M	Headache. Paresthesias of right side of face. Ptosis and fixed pupil. Hemiparesis on left. Papilledema	At origin	Dilation of right anterior portion of lateral ventricle
Elvidge, A. R., and Werner, A.: A. M. A. Arch. Neurol. & Psychiat. 66:752, 1951	6	M	Spells of not being able to walk for 3 wk. Headache progressed to speech difficulty and right-sided weakness. Motor aphasia and homonymous hemianopsia on right. Hemiparesis and extensor plantar response on right	Narrowing internal carotid artery in intracranial portion. Poor filling of middle cerebral and no filling of anterior cerebral artery	No treatment stated. Dilation of ventricles on air study
Shapiro, R.: Radiology 58:94, 1952	5	M	Difficulty speaking and right-sided weakness. Onset after coma of ½ hr. Aphasia, homonymous hemianopsia on right, and flaccid paralysis and extensor plantar response on right	Region of siphon*	No treatment. Speech and right side normal in 6 mo.
Richter, H. R.: Acta radiol. 40:108, 1953	5	M	Aphasia and hemiplegia on right for 2 days	At origin	No treatment or follow-up stated
Cabieses, F., and Saldias, C.: Neurology 6:677, 1956	9	M	Weakness of right side for 2 days	At origin	Artery explored. Ethyl biscoumacetate and papaverine given. Normal in 6 mo.
Goldstein, S. L., and Burgess, J. P.: A. M. A. J. Dis. Child. 95:538, 1958	7	M	Sudden coma. Later, aphasia and hemiparesis on right. Day later more alert. Then right-sided seizures. Died after angiography	3.5 cm. above origin	Died 2 days after admission after deepening coma
Davidson, D. T., and others: Tr. Am. Neurol. A. 82:102, 1957	1 infant; 3 older children		Hemiplegia of sudden or gradual onset; inflammation of paranasal sinuses presumed cause in 1	1, at origin; 3, at siphon	3, clinical recovery; 2, persistent block on arteriogram
Stevens, H.: Ann. Int. Med. 49:1022, 1958	5½	F	Spontaneous carotid artery thrombosis		Recovered without residuals
	13	Not given	Acute episode		Hemiparesis on left after 5 yr.
Murphy, F., and Shillito, J., Jr.: J. Neurosurg. 16:24, 1959	10	M	Aphasia and hemiplegia on right	At siphon	Artery explored. Incomplete recovery in 12 days

* Site of bend of carotid artery outside sella turcica.

ASSOCIATION OF MYXEDEMA HEART AND ARTERIOSCLEROTIC HEART DISEASE

Hermann Zondek, M.D., Jerusalem, Israel

When I first described the symptomatology of the myxedema heart 40 years ago[1] it was considered a rare variety of cardiac pathology. The myxedema heart is no longer a rarity. The increased rate of its reported incidence must be attributed to the great therapeutic advances made in the last decades in the field of thyroid disease, especially thyroid hyperfunction, such as antithyroid drugs and the clinical use of radioiodine.

The symptom complex of myxedema heart includes bradycardia, an often enormous dilation of the heart shadow, superficial heart contractions, a low cardiac output, flat or absent T waves with occasional lengthening of the Q-T interval in the electrocardiogram (ECG), soft heart sounds with correspondingly low waves in the phonocardiogram, and an abnormal venous pulse curve (absence of the auricular wave, a hump on the limb of the curve corresponding to ventricular systole, and complete absence of the normal diastolic fall). The latter two phenomena are only rarely referred to in the medical literature, although they are by no means less characteristic of the myxedema heart than the others.

The nature of the cardiac changes in myxedema is clearly demonstrated by the often dramatic effects of thyroid replacement therapy. In contradistinction to most other cardiac conditions, which at best only partially respond to adequate treatment, the various features of the myxedema heart regress promptly and fully as a result of thyroid medication. This response to therapy has been greatly accelerated by the recent introduction of thyroid substances such as sodium liothyronine and triiodothyroacetic acid which, having the same range of activity as the previously known ones, differ from them biologically only in the rapidity of their action. For example, in 1918 when I first studied the effects of thyroid substances on the myxedema heart, I found that 10 or 12 Gm. of desiccated thyroid given over a period of two months restored the size and function of the myxedema heart to normal. In 1928 I obtained the same results with 8 or 10 mg. of thyroxine, given over 20 days. In 1955 only 240 to 1,480 mcg. of sodium liothyronine, administered over 2 to 15 days, was required for the same purpose.

The reversibility of the cardiac alterations in myxedema argues against the long-held theory that the myxedema heart is a form of cardiac insufficiency rather than an essential, pathognomonic feature of the disease. Indeed, myxedema does not as a rule lead to cardiac insufficiency, even in untreated disease of long standing. It is true that, in an occasional patient, the myxedema heart and insufficiency of the heart muscle may coexist, but both must be regarded as distinct clinical entities requiring different therapeutic approaches. This is also true of the joint occurrence of the myxedema heart and coronary obliterating processes, e. g., arteriosclerosis (although myxedema, if untreated, may predispose toward arteriosclerosis). This combination is not always readily evident, as precordial pain may also occur in myxedema, and electrocardiographically the myxedematous alterations may mask the presence of other morbid phenomena which will be detected only after the former have cleared up as a result of specific therapy. A relevant case will be briefly reported.

Report of a Case

A 46-year-old woman complained of heaviness, obstinate constipation, and anginal pain, the latter being unresponsive to the usual therapy with coronary dilators.

Examination revealed, besides evidence of cardiovascular arteriosclerotic disease (blood pressure 170/90 mm. Hg, accentuation of the second aortic sound and a systolic murmur over the aorta, and dilatation of the aorta in which several sclerotic plaques were seen), the signs and symptoms of myxedema: typical outward appearance and behavior, dry skin, hoarse voice, slow speech, and sluggish Achilles-tendon reflexes. The basal metabolic rate was –23%; serum cholesterol level was 266 mg.%; the heart was dilated to both sides, though more to the left than to the right; and the electrocardiogram showed low voltage with flat or absent T waves. There was however no bradycardia (pulse rate between 72 and 86 per minute).

The patient received sodium liothyronine in daily doses of 120 mcg. for the first four days; thereafter the dosage was gradually reduced. As a result of substitution therapy a clinical remission, including a noticeable reduction in size of the heart shadow, was promptly achieved. One of the first signs was the disappearance of the myxedema pattern in the ECG after two days of therapy, i. e., after the administration of 240 mcg. of sodium liothyronine. In its stead a strain pattern became evident on the left side. It was concluded that this had been masked by the predominant myxedematous alterations, which are assumed to result from watery imbibition of the heart tissue. The precordial pain subsided after the administration of 660 mcg. of sodium liothyronine in seven days.

After regression of the myxedematous symptoms the patient's condition was satisfactorily controlled with administration of 0.1 Gm. of desiccated thyroid four times per week. As a rule only small maintenance doses are required and tolerated by patients with associated arteriosclerotic disease and myxedema. Larger doses are apt to provoke a recurrence of the precordial pain in such patients, although on different pathogenic grounds.

It is worthy of note that the pulse rate, blood pressure, and serum cholesterol level remained unchanged throughout the entire course of observation in this patient. This lack of response to specific therapy must be attributed to irreversible changes in the cardiovascular system and serum lipid levels brought about by the associated arteriosclerotic disease, as frequently observed in patients with untreated myxedema.

Summary

A 46-year-old woman complained mainly of anginal pain which was refractory to the administration of the commonly employed coronary dilators. Examination revealed, in addition to evidence of cardiovascular arteriosclerotic disease, the presence of myxedema including the characteristic electrocardiographic alterations of the myxedema heart. A prompt and full regression of the myxedematous symptoms was achieved with administration of sodium liothyronine. The myxedema pattern in the electrocardiogram disappeared after the patient had received 240 mcg. within two days, and a left strain pattern, previously masked by the myxedema, was found. The precordial pain subsided after seven days of substitution therapy. Subsequently the patient was kept in a euthyroid and clinically satisfactory state with administration of 0.4 Gm. of desiccated thyroid per week.

8 Maimon St.

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HUGE OSTEOMA OF THE ELEVENTH LEFT RIB

Israel Steinberg, M.D., New York

A huge osteoma of the 11th left rib had been present for over 50 years in a 71-year-old man. Operation had been recommended on many occasions but had been refused because the growth had caused the patient no discomfort. The roentgenographic appearance of the tumor suggested an osteoma which involved the rib and extended into the left pleural cavity above and retroperitoneally into the abdomen below. The histological nature of the tumor was confirmed when the patient died of hemorrhage due to cancer of the right kidney. This case is deemed worthy of report because of the unusually large size of the osteoma (3.5 lb.), its benign course, and the unusual appearance of the chest roentgenogram.

Report of a Case

A 71-year-old man was first admitted to the New York Hospital–Cornell Medical Center on Jan. 16, 1952, with the complaint of urinary retention. This symptom had first occurred 16 years prior to admission and had been completely relieved by transurethral prostatectomy performed at another hospital. He had remained well until onset of frequency, urgency, and nocturia two weeks prior to coming to this hospital. The patient recalled injuring the lower left part of his chest while doing calisthenics 51 years prior to admission; the next year a mass in the left flank was called to his attention. Since it had caused no symptoms, he had paid little attention to it. At another hospital, in 1936, he was urged to have the mass excised, but he had refused.

Physical examination showed a well-developed and well-nourished man in mild distress because of urinary retention. Rectal examination revealed an enlarged prostate. A large (15-by-15 cm.), stony hard, nontender, fixed mass was felt in the left flank beginning under the rib cage and almost reaching the iliac crest. There was increased anteroposterior diameter of the chest; the heart was not enlarged to percussion. A soft apical systolic murmur was heard; the blood pressure was 170/100 mm. Hg. The electrocardiogram was normal except for an increased QRS interval due to bundle-branch block. Bilateral inguinal hernia and varicose veins of the left leg were also found.

Roentgenographic examination of the chest showed slight enlargement of the left ventricle and elongation and tortuosity of the thoracic aorta

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From the Department of Radiology, the New York Hospital–Cornell Medical Center.

(fig. 1, *left*). A huge, lobulated, calcified mass was seen in the left lower posterior lung field. A film of the lower left part of the thorax (fig. 1, *right*) showed the mass to measure 18 by 12 cm., and flaring and distortion of the left 11th rib was evident. The mass contained mottled, calcific deposits and extended retroperitoneally, displacing and distorting the left kidney (fig. 2).

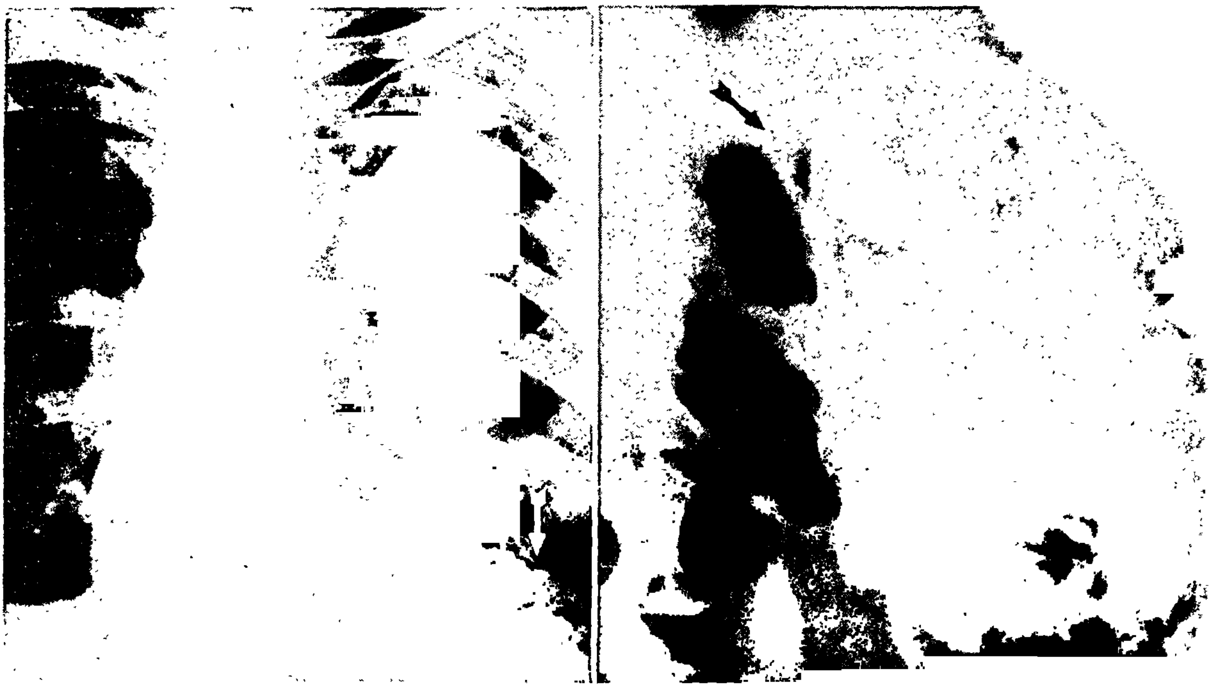
Fig. 1.—*Left*, frontal teleroentgenogram of chest showing calcific mass at left costophrenic angle (*arrow*). Heart is enlarged, ascending aorta is dilated, and aortic knob is prominent. *Right*, roentgenogram of lower thoracic cage showing huge lobulated (18 by 12 cm.) mass containing calcium; 11th left rib is flared and distorted (*arrow*).

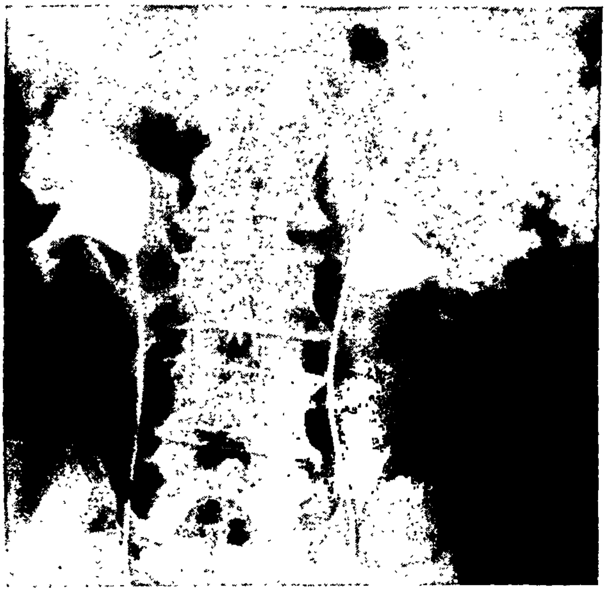
Fig. 2.—Retrograde pyelogram showing displacement of left kidney by calcified mass.

After the usual preliminary urologic studies, a transurethral prostatectomy was performed on Jan. 23, 1952. A left inguinal hernioplasty was also done on Feb. 1, 1952. On Feb. 8, 1952, the patient was discharged as improved.

Over four years later, Oct. 26, 1956, the patient was readmitted to the emergency service because of sudden onset of severe hematuria and colicky pain in the right inguinal region. Examination showed an acutely ill and dyspneic man. There were scattered rhonchi over the lungs. The hemoglobin level was 90% and the blood pressure 165/80 mm. Hg. A huge, stony, hard tumor in the right upper quadrant was again palpated. Ten ounces of blood-stained urine and clots was removed from the bladder. An hour later the patient became comatose and died suddenly.

Autopsy examination revealed extensive carcinoma of the right kidney, the greater part of which was destroyed by hemorrhage; a massive perirenal hematoma measured 20 by 15 by 6 cm. The left kidney was small and showed arteriosclerosis and arterionephrosclerosis. There was also arteriosclerotic heart disease with enlargement of the left ventricle which measured 2.2 cm. in thickness. General coronary arteriosclerosis was present with foci of fibrosis in the myocardium on microscopic examination. The lungs showed pulmonary edema, hyperemia, marked pulmonary emphysema, and bronchiectasis. Nodular hyperplasia of the prostate and chronic prostatitis were also found.

An ovoid, stony, hard mass in the left posterior pleural cavity measured 17 by 13 by 11 cm. and weighed 1,640 Gm. (3.6 lb.). It was attached to the 11th rib and had a bony shell; on the cut surface it appeared variegated and contained mixtures of bone, cartilage, and fat (fig. 3, *left*). Microscopically, pink, loose, fibrillar tissue was interspersed with bony spicules and foci of calcification and clumps of fat cells were seen (fig. 3, *right*).

Comment

In this era of modern surgery, tumors near the surface of the body are usually excised before they attain a large size. Although the mass described above was first noticed when the patient was 20 years of age, the usual time of discovery of osteomas,[1] he refused operation. At death, 50 years later, it had become huge but remained benign. Although the tumor distorted the rib at its origin, reached into the left pleural cavity and retroperitoneal space, and displaced the left kidney, it did not interfere with kidney function.

Osteomas arising from ribs are apparently not uncommon.[1] However, only one other example similar to the one herein reported could be found in the literature. Hodges and associates,[2] in their chapter on the roentgen diagnosis of diseases of bones, describe and illustrate an osteochondroma of the left 11th rib that occurred in a 19-year-old woman. Judging from the roentgenogram and photograph of the specimen, that tumor was smaller than the one described above. Also, the tumor in their case had been present only for four years prior to excision.

Summary and Conclusions

A 3.5-lb. osteoma had been attached to the 11th rib of a 71-year-old man for 50 years. Roentgenographic study of the tumor showed it to arise from the 11th left rib and contain calcium and bone; this readily established the diagnosis of osteoma. The tumor was located in the gutter of the left pleural space, causing findings on roentgenogram of the chest to stimulate a pulmonary mass. Despite the large size and displacement of the left kidney, the tumor remained benign; death was due to carcinoma of the opposite kidney.

525 E. 68th St. (21).

The Department of Pathology gave permission to report the pathological data in this study.

This study was aided by a grant from the Mallinckrodt Chemical Works, St. Louis.

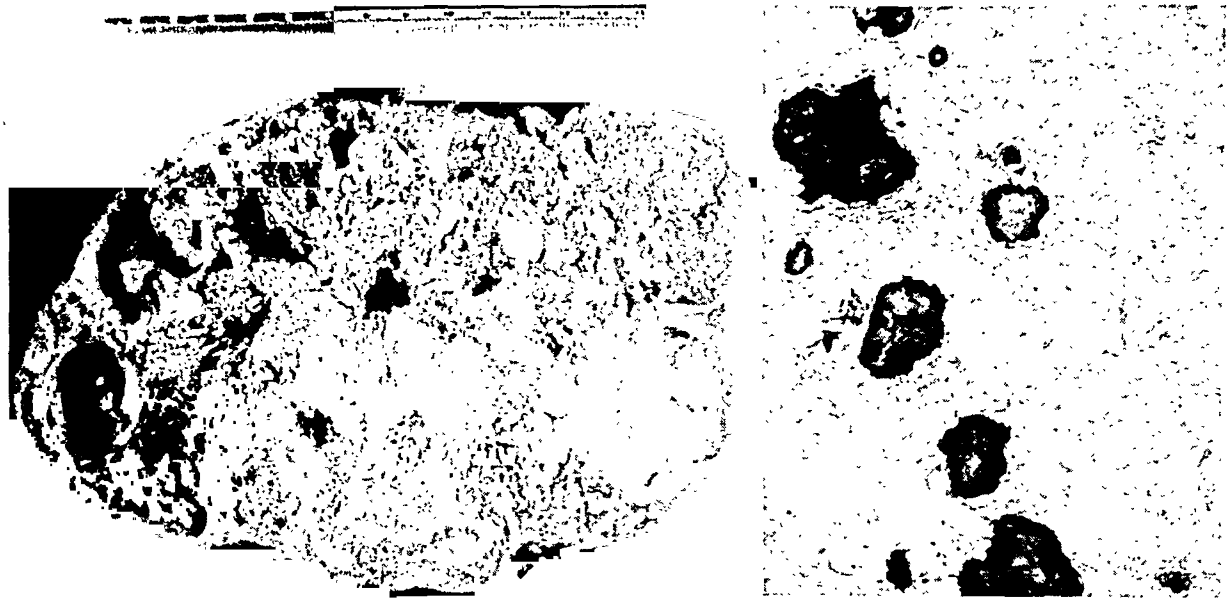

Fig. 3.—*Left,* cut section of gross specimen showing stony hard mass with bony shell. *Right,* photomicrograph shows areas of calcification in acellular fibrous tissue (hematoxylin-eosin stain; × 60).

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EXCHANGE TRANSFUSION FOR ASPIRIN POISONING

Thomas L. Sterne, M.D., Victoria, Texas

This is a case report of a 6-week-old infant treated for aspirin intoxication by exchange transfusion. It is presented to call attention to the dangers of excessive aspirin administration and also to an emergency treatment. Despite a voluminous literature on the danger of salicylate intoxication, the average mother and many doctors still prescribe this drug as though it were harmless. Until such time as the entire medical profession and the general public become aware of the problem, we will continue to have unnecessary deaths caused by one of the most valuable drugs that we have available. The labeling of salicylates as potentially harmful is not sufficient to prevent overdosage, and the so-called safety caps on children's aspirin do not prevent accidental poisoning.

Report of a Case

A 6-week-old male infant was admitted to the DeTar Memorial Hospital on Dec. 24, 1958, at 11 p. m., with the history of an upper respiratory tract infection for two days, with progressive dyspnea. He had had a convulsion just prior to admission. His mother had given him a total of 12 grains (0.75 Gm.) of aspirin during the previous 48-hour period, but no other treatment had been given. Fluid intake had been poor.

On admission he had temperature of 103.5 F (39.8 C) rectally; his pulse rate was 180 per minute and respirations were 48 per minute. He appeared dehydrated and dyspneic. He was in opisthotonos and was cyanotic. A lumbar puncture was attempted, but no fluid was obtained. An x-ray on admission showed emphysema and one small area of increased density in the upper lobe of the right lung. His hemoglobin level was 9.5 Gm.%, with a hematocrit value of 24%; the leukocyte count was 20,100 per cubic millimeter, with a differential count of 65% segmented forms, 2% stab cells, and 33% lymphocytes. The carbon dioxide content was reported as 56 vol.%, chloride level 133 mEq. per liter, blood salicylate level 23 mg.%.

The patient was started on therapy with antibiotics, calcium gluconate, intravenously given fluids, and sedation for convulsions. He received a transfusion of 100 cc. of blood and vitamin K parenterally. During the night his convulsions were controlled and his respirations became less labored; he was improved the next morning but was voiding very little. At that time his carbon dioxide content was 44 vol.% and chloride level 103 mEq. per liter.

I first saw the infant at noon Dec. 25, 1958, because he was again having mild tonic seizures, was in constant purposeless motion, and was fretting, extremely dyspneic, and cyanotic, despite therapy with oxygen. At that time his blood pH was 7.9. He appeared well hydrated but was voiding only a few drops infrequently. His salicylate level at that time was 35 mg.%.

An exchange transfusion was done, using type-specific blood. His initial venous pressure was 30 cm. of blood at the umbilicus. A total of 310 cc. of blood was given and 420 cc. removed in 10-cc. portions. During the exchange his respiration rate slowed slightly, but the dyspnea was still marked. His general condition seemed slightly improved after the exchange. Venous pressure was still 30 cm. at the end of the exchange, despite a deficit of 110 cc. His salicylate level at the completion of the exchange was 29 mg.%. For these reasons a second exchange was done a short time later.

His venous pressure at the second exchange was 14 cm. at the beginning and 11 cm. at the end. A total of 475 cc. of blood was removed during the exchange and 500 cc. was replaced. His respiration and general condition improved during the second exchange, and at discontinuation of oxygen therapy he was without cyanosis. At that time his cry was very good and he slept quietly when left alone. His salicylate level was 23 mg.% after the second exchange.

By the next morning the infant looked very well, was voiding adequately, and was taking fluids by mouth. Blood examination showed the hemoglobin level to be 11.4 Gm., the hematocrit value 35%, and the white blood cell count 8,400 per cubic millimeter, with 68% lymphocytes and 32% segmented forms. He was discharged on the fourth hospital day and had no further difficulty.

Comment

Recently there have been many reports of salicylate poisoning, with much emphasis on methyl salicylate. In actual numbers of patients receiving an overdosage of any form of salicylates, aspirin poisonings outnumber many times those of any other salicylate. Infants and small children are especially prone to develop symptoms from accidental overdosage or iatrogenic causes. They are easily dehydrated by the primary illness, which prompts the administration of the aspirin, and are often oliguric. Approximately 20% of ingested salicylate is destroyed in the tissues; the remainder is excreted by the kidneys. If there is inadequate urinary output, there is, of course, inadequate elimination of the drug. If inadequate elimination is combined with overdosage, symptoms may appear rapidly, especially in young infants whose renal function is not fully developed.

Cann and Verhulst [1] have given an excellent discussion of salicylate poisoning that thoroughly covers the subject. They review the pharmacology, pathophysiology, and presently accepted method of treatment in a very readable, concise, and accurate manner.

No explanation can be given for the presence of alkalosis approximately 24 hours after the last dose of aspirin in the patient reported here, since usually acidosis replaces alkalosis within six to eight hours. This and his failure to respond to more conservative measures probably were the results of his oliguria. It was felt that the exchange transfusion in this case not only removed salicylate from the body but also corrected the electrolyte imbalance.

The mainstay in the treatment of salicylate poisoning consists of giving fluids intravenously to correct the existing water deficit and maintain adequate urinary output. Other details of therapy are fully covered by Cann and Verhulst.[1]

If more conservative measures fail, hemodialysis should be seriously considered. Even though the number of institutions offering this procedure is increasing, there are many areas where it is not readily available. An exchange transfusion readily accomplishes the same result and can be performed in any hospital where fresh blood is available. This is particularly adaptable to infants and young children because of the small circulating blood volume.

Summary and Conclusions

A young infant had acute salicylate intoxication which failed to respond to fluid and electrolyte therapy. He was treated by two successive exchange transfusions. Recovery followed without incident. This method of therapy is proposed under these circumstances in young infants when hemodialysis cannot readily be done.

2701 N. Azalea.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. Kautz, M.D., *Secretary.*

This report was prepared by the Subcommittee on Blood Dyscrasias to bring to the attention of the medical profession the existence of the Registry on Blood Dyscrasias.

Norman De Nosaquo, M.D., *Secretary,*
Committee on Research.

DEVELOPMENT AND PURPOSE OF THE REGISTRY ON BLOOD DYSCRASIAS

An increasing number of drugs and other potentially toxic compounds found in industries, in the home, and in our daily contact are being introduced every year. Untoward reactions to some of these substances may be so rare as to avoid detection, even after careful field test prior to release to the public. Although these reactions may be rare, they can be very serious on occasion. This is particularly true of the drug-induced blood dyscrasias. It is impossible to differentiate clinically between a case of drug-induced marrow depression and one which apparently occurs spontaneously.

An investigator working independently might have difficulty assessing accurately the occasional hematological ill-effect he may see from the use of a drug. However, the collective experience of a number of observers may be helpful. For this reason, the Registry on Blood Dyscrasias of the Committee on Research of the American Medical Association was established to assemble reports of blood dyscrasias in which drugs and toxic agents conceivably played a role. The registry is intended as a means of alerting the medical profession to such possibilities. It is not meant to be a repository for authoritative or statistical information.

The Subcommittee on Blood Dyscrasias conducted a two-year pilot study and has reviewed the accumulated data. It has concluded that this information could serve as an early warning system for the medical profession. The summaries, which are prepared semiannually, will be distributed widely, in the hope that physicians will become aware of the existence of the registry and will report cases. The current summary has been distributed to the following groups: state and county medical societies, hospitals, medical school libraries, and departments of pharmacology, pathology, medicine, and pediatrics of all medical schools. Physicians may examine this information at these sources, or they may write to the Committee on Research, American Medical Association, for copies. In the summary for the second half of 1958, 427 cases have been reported to the registry by physicians in the United States and Canada since 1953, and some cases have been taken from the literature. Reports are accepted by the registry only when the drug or toxic agent was administered to the patient within six months prior to the appearance of the dyscrasia. It is evident that inclusion of a drug in the list does not necessarily mean that it is harmful or that it was the cause of the reported dyscrasia. The information contained in the summary is not to be considered authoritative or statistically significant, since these data are "raw" and undoubtedly represent only a small segment of the total number of cases which probably occur.

When a patient develops a blood dyscrasia after use of a single drug, there is stronger circumstantial evidence of an etiological relationship than in instances in which many drugs were administered. If it is well known that one of the drugs administered may cause the dyscrasia, suspicion should not rest as heavily on the other drugs, especially if they are not known to cause a dyscrasia.

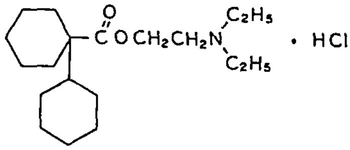
The continued effective operation of the registry depends on the cooperation of physicians who have seen patients with blood dyscrasias which they suspect might have been induced by a drug or toxic agent. The form used in reporting cases to the registry may be obtained by writing to the Secretary, Committee on Research, American Medical Association, 535 N. Dearborn St., Chicago 10.

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Dicyclomine Hydrochloride (Bentyl Hydrochloride).—2-Diethylaminoethyl bicyclohexyl-1-carboxylate hydrochloride.—The structural formula of dicyclomine hydrochloride may be represented as follows:



Actions and Uses.—Dicyclomine hydrochloride is a synthetic anticholinergic drug which is used clinically for its atropine-like effects on the gastrointestinal tract. It acts both on neuroreceptor sites innervated by postganglionic parasympathetic fibers and directly on smooth muscle tissue; there is no evidence for ganglionic blockade. After oral or parenteral administration to animals, dicyclomine causes a delay in gastric emptying, inhibits the propulsive motility of the small intestine, partially relieves morphine-induced spasm of the sphincter of Oddi, strongly antagonizes the intestinal effects of acetylcholine and related cholinergic compounds, and exerts a mild inhibiting effect on the tonus of the isolated dog ureter. In these respects, the drug is less potent than atropine. It is much less potent (1/300 to 1/400) than atropine in mydriatic or antisialogogue action and is virtually free of the cardiac effects of the belladonna alkaloids. Dicyclomine exerts little, if any, gastric antisecretory effects.

Dicyclomine hydrochloride is used for the symptomatic management of functional disorders of the gastrointestinal tract which are characterized by hypermotility and spasm and which may occur as a primary disturbance. Since the drug exerts a spasmolytic effect on the lower as well as the upper portions of the intestine, it may be used in functional intestinal distress (irritable colon, spastic constipation, mucous colitis, spastic colitis). It is also proposed for use in pylorospasm and biliary dyskinesia, but, in view of the questionable clinical status of these functional diagnoses, the usefulness of anticholinergic therapy in such cases is uncertain. There is little convincing evidence that antispasmodics such as dicyclomine are of value in the management of cardiospasm.

The drug may also be used as an adjunct in the therapy of certain organic diseases of the gastrointestinal tract. These include peptic ulcer, ulcerative colitis, and diverticulitis. Since dicyclomine does not inhibit gastric secretion, concomitant administration of antacids is imperative when the drug is used in the treatment of duodenal ulcer. The value of anticholinergic drugs, including dicyclomine, for the treatment of esophagitis, gastritis, duodenitis, and cholecystitis is considered dubious. Likewise, there is little rationale for the employment of such agents in patients with asymptomatic diverticulosis or hiatal hernia; complications arising from such conditions are predominantly surgical, rather than medical, problems.

Dicyclomine is virtually free of some of the more troublesome atropine-like side-effects, thus permitting more general use of the drug in conditions in which secretory inhibition is not of the first import. In the doses used clinically, mydriasis or cycloplegia has not been a problem. The drug can safely be used in patients known to have glaucoma. It likewise causes little xerostomia. Urinary retention in patients with prostatic hypertrophy has not been encountered. In occasional instances, patients may complain of slight dizziness and a feeling of abdominal fulness or experience brief periods of euphoria. It is contraindicated in patients with frank urinary retention, stenosing peptic ulcer, and pyloric or duodenal obstruction.

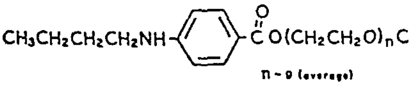
Dosage.—Dicyclomine hydrochloride is administered orally or intramuscularly. By either route, the usual dose is 20 mg. for adults, 10 mg. for children, and 5 mg. for infants. The frequency of administration varies from three to four times a day. Some adult patients with severe gastrointestinal spasticity or hypermotility may require doses of 25 to 37.5 mg. three times daily for adequate relief of symptoms.

Preparations.—capsules 10 mg.; solution (injection) 20 mg. in 2 cc., 100 mg. in 10 cc.; syrup 2 mg. per cc.

Year of introduction: 1950.

The Wm. S. Merrell Company cooperated by furnishing scientific data to aid in the evaluation of dicyclomine hydrochloride.

Benzonatate (Tessalon).—ω-Methoxypoly(ethyleneoxy)ethyl *p*-butylaminobenzoate.—The structural formula of benzonatate may be represented as follows:



Benzonatate is a pale yellow, viscous liquid.

Actions and Uses.—Benzonatate was introduced in 1956 as an antitussive agent. It is chemically related to the local anesthetic, tetracaine, by replacement of the dimethylamine group with a methylated polyethylene glycol, and is one of a number of derivatives of local anesthetics screened for relatively high specificity toward sensory receptors of vagal afferent fibers involved in the production of cough. It is postulated that, after systemic absorption, benzonatate produces an inhibitory effect on these peripheral structures similar to that which would result from topical application of a local anesthetic to the respiratory mucosa. However, benzonatate also acts upon the central nervous system, since it inhibits transmission of impulses of the cough reflex in the vagal nuclei of the medulla and strongly depresses polysynaptic spinal reflexes. The relative importance of the peripheral and central activity of benzonatate in producing its antitussive effects in man remains to be determined.

Benzonatate has been reported to inhibit cough experimentally induced in animals by insufflation of soap powder and in man by inhalation of aerosols of citric acid solutions, with approximately the same efficiency as codeine. Unfortunately, benzonatate seems relatively less effective against the cough associated with clinical illness than against that induced artificially, when it is compared with codeine.

On the basis of early clinical trials, it may tentatively be concluded that benzonatate is effective in some patients in suppressing, to a varying degree, cough due to acute or chronic bronchitis and tracheitis, pulmonary tuberculosis, bronchiectasis, advanced emphysema, early bronchogenic carcinoma, and bronchial asthma. It appears to be ineffective in preventing the cough associated with bronchoscopy and other manipulative procedures. Reports concerning the effects of benzonatate on the volume and character of respiratory secretions are conflicting; there is no definite proof that it is an expectorant.

In contrast to codeine and other opiate antitussives, benzonatate does not depress respiration. On the contrary, in bronchial asthma, it is reported to increase rate and depth of respiration and respiratory minute volume; vital capacity is also augmented. Subjective relief of dyspnea is often reported, despite this respiratory stimulation and despite the fact that rate of expiratory flow is not altered. Similarly, in pulmonary fibrosis and emphysema, improvement is seen in exercise tolerance, accompanied by an increase in tidal volume, but without any change in expiratory velocity. Here, however, no significant alteration of vital capacity occurs.

When given by mouth, benzonatate produces no detectable effect on the cardiovascular system. Even after intravenous injection, benzonatate has little effect, although a small, transitory rise in blood pressure sometimes occurs.

When given orally, effects may occur within 10 to 20 minutes and last two to eight hours.

Benzonatate is well tolerated in therapeutic doses. No reports of serious toxicity have yet appeared. The total incidence of side-effects is low. Among those reported are drowsiness, nausea, skin eruption, nasal congestion, dizziness, and a sensation of burning of the eyes and of numbness or tightness in the chest. If the capsules are allowed to dissolve in the mouth, they exert a local anesthetic effect on the mucosa that is disagreeable to a few patients. Side-effects characteristic of those caused by codeine and other narcotic antitussives are largely absent. Habituation, euphoria, respiratory depression, or constipation have not been reported.

Benzonatate may be used for the symptomatic relief of cough. It must be remembered, however, that suppression of a productive cough may be harmful in some cases and that such suppression is usually inadvisable in the immediate postoperative period. In such instances, the use of benzonatate or other antitussive agents is contraindicated. For the present, the use of benzonatate for the relief of dyspnea must be regarded as experimental.

If further clinical investigations confirm early reports, benzonatate may be regarded as a valuable addition to the available antitussives and one which is notably free from serious toxicity. Regrettably, much of the information now available is drawn from isolated case reports and clinical experiments of which the experimental designs are subject to criticism. Since there have been only a few controlled investigations comparing benzonatate with other antitussive agents, no definite statement can be made regarding its efficacy relative to other drugs of this type.

Dosage.—Benzonatate is given orally. The suggested dosage is 100 mg. given three to six times daily. The capsules should not be chewed.

Preparations: capsules 50 mg. and 100 mg.

Ciba Pharmaceutical Products, Inc., cooperated by furnishing scientific data to aid in the evaluation of benzonatate.

COUNCIL ON FOODS AND NUTRITION

PROGRAM OF THE COLUMBIA UNIVERSITY INSTITUTE OF NUTRITION SCIENCES

W. Henry Sebrell Jr., M.D., New York

Physicians and members of the allied professions specially trained in the field of public health are needed badly. Many universities offer a curriculum and encouragement to the student both from the United States and from foreign lands in the field of public health. Tulane University Medical School, the University of Pittsburgh, Harvard University School of Public Health, and Vanderbilt University School of Medicine, for example, can accommodate the student who finds an interest in the field of international nutrition. The Institute for Nutrition Sciences at Columbia University has been developed especially to meet this need. When, in the preliminary stages of development of this institute, it became obvious that a person must be chosen as director who had the unique qualities of devotion to public health, a wide experience in the field of nutrition, and the foresight for devising a program that could be followed through many years, Dr. W. Henry Sebrell Jr. was selected as that director. The Council on Foods and Nutrition is pleased to call attention to this new school at Columbia and will encourage its further development. The Council has authorized publication of the following report about this program.

PHILIP L. WHITE, SC.D., *Secretary.*

Malnutrition adversely affects the life, development, and health of more people in the world than any disease. It kills millions of infants and small children and stunts the development of millions of other children, especially in the technically underdeveloped areas. Metabolic diseases, which can be controlled to some extent by nutritional management, are also of major concern in the nondeveloped countries. Yet, there are only a few physicians and public health workers who have been trained to deal effectively with the problem. This world shortage of people adequately trained in the public health aspects of nutrition is a serious handicap to progress in improving nutrition in all countries. Such people are needed both by the United Nations organizations and by national governments and departments of health.

Recognizing this need and seeing the great opportunity to meet the situation, Dr. C. Glen King, through the resources of Columbia University, planned and organized the Institute of Nutrition Sciences. Dr. King, who is a member of the faculty of Columbia University and director of the Nutrition Foundation, Inc., served as the institute's acting director until last year. Dr. King will continue his close personal interest as a member of the faculty committee and the advisory board. The first students were accepted in September, 1958.

The Institute of Nutrition Sciences, although primarily a graduate teaching institute, will conduct a broad research program as an essential part of adequate graduate instruction and to fulfill the need for additional knowledge about human nutrition. Since the program of the institute is oriented toward public health, it is placed administratively in the School of Public Health and Administrative Medicine, but students may take courses as needed in any part of the university or its affiliated organizations.

The program of study is organized to teach the student the underlying causes of malnutrition, the extent and distribution of the various kinds of

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Director of the Institute of Nutrition Sciences, Columbia University.

malnutrition, the procedures for conducting an assessment of human nutrition, and the diagnosis, treatment, and prevention of malnutrition. A graduate of the institute will be competent to plan and carry out comprehensive public health nutrition programs of national scope and will be able to understand the complex international problems in the production and movement of foods. Insofar as we know, such a course is not now available anywhere else in the world. The instruction includes courses on food production and agricultural economics, food technology, food laws and regulations, biochemistry and food chemistry, human nutritional requirements, biostatistics, health education, epidemiology, the assessment of nutritional status, deficiency diseases and their control, the social aspects of nutrition, and the management of national and international public health nutrition programs.

A course of study will be selected to meet the needs of the individual student on the basis of his past training and experience, as well as the work he plans to do and the country in which he plans to work. The degrees being offered are an M.S. in nutrition and a Ph.D. in nutrition. A special course for physicians is being developed which will enable the student to obtain an M.P.H. and an M.S. in nutrition within 18 months. The M.S. degree is intended primarily for those students who anticipate working on the public health problems of nutrition, especially in technically underdeveloped areas. The Ph.D. is, of course, intended for the advanced student of exceptional ability who can meet the requirements in the basic sciences and modern languages in addition to carrying out an original investigation leading to a satisfactory thesis.

However, the program differs from most academic programs in nutrition in that three months of field work in nutrition is a requirement for any of the degrees. This field work also will be planned on an individual basis and will vary widely in location and type, ranging from work in a state or a large city health department to a national health department or a village in a technically underdeveloped area. In order to carry out such a program adequately, the institute has already initiated plans for cooperative training and study with research and educational institutions and health organizations in several parts of the world. It is anticipated that many of the students will be from foreign countries and will want to learn to deal with malnutrition as it exists in their own country. Since these problems and their solutions are so widely varied, several training centers will be necessary in different parts of the world. It is therefore anticipated that the program of the institute will be international in its scope, although centered in Columbia University.

The research program is planned as an adjunct to the teaching program and will be conducted in three main categories. The first of these will be field studies dealing with nutrition surveys, the assessment of nutritional status, problems in controlling malnutrition, and similar work. This area is under the direct supervision of Dr. Elmer L. Severinghaus, professor of public health nutrition. An extensive survey was carried out in Haiti during the past summer, and the data are now being prepared for publication. A cooperative project is under way in Puerto Rico, and others are being planned.

The second main research area is in that of human metabolic diseases and their relation to nutrition. This area of research is under way in St. Luke's Hospital in New York City in collaboration with and under the direction of Dr. Theodore B. Van Itallie, medical director and assistant in medicine and with Dr. W. Henry Sebrell Jr., director of the institute and a consultant in nutrition at St. Luke's Hospital. This program involves controlled metabolic studies on patients with various diseases such as atherosclerosis, arteriosclerotic heart disease, and diabetes. A metabolic unit and beds for special studies, with the necessary supporting biochemical laboratories and research animal facilities, are available.

The third main area of research is that of fundamental biochemical work in nutrition. Since new laboratory facilities are required, this is now in the planning stage. The architect's drawings have been completed, and it is anticipated that the program will be under way in less than a year.

Since the institute represents a new educational venture of potentially great international significance, an advisory board has been created which consists of distinguished and well-qualified citizens with broad international interest. This advisory board is under the honorary chairmanship of the Honorable Herbert Hoover. The active chairman is Mr. Clarence Francis, consultant to President Eisenhower on agricultural and food problems. Other members of the board are:

Joseph W. Barker
Ernest T. Baughman
Leona Baumgartner
Frank Boudreau
William T. Brady
Leroy E. Burney
George H. Coppers
T. L. Daniels
Thomas C. Desmond
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Benjamin Strong
C. Cullen Thomas

The institute, with such able guidance, should make a significant contribution to preventive medicine throughout the world.

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POSTGRADUATE CONTINUATION MEDICAL EDUCATION

IN ITS efforts to be of assistance to members of the medical profession in their continuing education, the Council on Medical Education and Hospitals presents its annual list, Postgraduate Courses for Physicians, in this issue of THE JOURNAL for the year beginning September 1, 1959. Unlike the lists of medical schools, internships, and residencies published in THE JOURNAL, the information on postgraduate courses does not carry either approval or disapproval by the Council of the programs listed, and such should not be inferred by the reader.

The *ad hoc* Advisory Committee on Postgraduate Medical Education has recommended to the Council that a mechanism should be developed and implemented for the appraisal of the postgraduate educational resources of institutions and organizations active in this field. The Committee and the Council staff have been developing and pilot-testing such a mechanism during the past two years. A large-scale test is now in progress. If the appraisal mechanism under study is proved to be a valid and feasible approach for the preparation of a selective listing, then such data and recommendation will be considered by the Council. Such a selective list of postgraduate courses, if authorized, would provide a central reference of those educational programs sponsored by institutions and organizations having adequate postgraduate educational resources in terms of the basic principles[1] published two years ago.

It is the consensus that worthwhile educational programs more effectively utilize the physician's time and are likely to whet his appetite for participation in other educational programs. Conversely, those programs lacking sufficient advance planning or utilizing pedestrian approaches that are relatively less effective educationally often discourage the participating doctor from continuing his education in other courses.

The recently published geographically oriented study of postgraduate courses and enrollments[2] demonstrated that doctors of medicine travel relatively great distances to postgraduate courses, and especially to those located in medical schools and their teaching hospitals. The facilities and personnel at medical schools and other medical centers are to an increasing extent utilized in an educationally meaningful manner in postgraduate courses, including an annually increasing number of individually arranged postgraduate traineeships in various fields. It seems reasonable to believe that there is a large potential demand on the part of the medical profession for a greater number of better postgraduate courses to help them remain abreast of the deluge of new knowledge. The Council hopes that the appraisal mechanism now under study will make it possible for future listings to indicate that the courses included are all likely to be worth the expenditure of time, intellectual energy, and money by the medical profession.

A major objective of the Council in its long-range planning relative to the continuing education of the medical profession has been and is to secure information that will be useful to all concerned as well as to identify and stimulate constructive action. That publication of an annual listing has been widely accepted is indicated by the fact that information on nearly all of the courses eventually coming to the attention of the Council office is submitted sufficiently in advance for inclusion in the list. This represents a constantly greater and more desirable degree of advance planning.

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[1] Guide Regarding Objectives and Basic Principles of Postgraduate Medical Education Programs, Council on Medical Education and Hospitals, American Medical Association, June, 1957.

[2] Council on Medical Education and Hospitals, Geographically Oriented Study of Postgraduate Courses and Enrollments in the United States for Physicians During the Year 1956-1957, J. A. M. A. **170**: 206-219 (May 9) 1959. (Available in limited numbers in reprint form with maps used.)

An innovation this year to make the list more useful is inclusion of a geographical cross-reference list in order that courses offered in each city may be more readily found in the listing.

THE AUTOCLAVE AND CROSS-INFECTION IN HOSPITALS

The problem of who is responsible for sterilization of supplies and equipment in hospitals has been studied by the Working Party of the Medical Research Council of London, England.[1] Their report is based on extensive and detailed investigations into existing arrangements for sterilization of surgical equipment in hospital wards, surgical units, sterile-supply departments, laboratories, and pharmacies in England.

Other recent publications[2] point out the importance of good housekeeping in hospitals—the need of more intensive application of the standard concept in aseptic and antiseptic methods in order to control the incidence of staphylococcus infection.

The possibility that cross-infection can take place in autoclaves is recognized. The Working Party in England concluded that, while there were a number of underlying factors for faulty sterilizing procedures by heat, two important factors usually stood out, namely: 1. There was a lack of understanding of the technical requirements involved in sterilizing by autoclaves. 2. No one member of the medical staff was given the final responsibility for overseeing the sterilizing procedure. The battle of asepsis can be won only by continual diligent application of the correct technique and by perpetual awareness and persistent observation by the physician in charge of sterilizing procedure. According to the directions for the correct operation of the autoclave, to kill the most resistant bacteria and their spores the air should be removed from the interior of the autoclave and the contents exposed to saturated steam at a pressure of 20 lb. per square inch (1.4 kg. per square centimeter) (126 C) for as long as 30 minutes. The Working Party found the use of a vacuum to remove the air less effective (unless used correctly) than the downward-displacement, that is, making sure the air is displaced by steam in the sterilizers. The personnel in charge of operating the autoclave should be trained and made aware of the problems and technique. The essential criticism in most instances has been divided responsibility, and the remedy clearly is to put one competent person in charge.

NEW REGISTRY ON BLOOD DYSCRASIAS

A report in this issue of The Journal (page 1925) outlines the purpose of a registry sponsored by the Subcommittee on Blood Dyscrasias of the Committee on Research of the Council on Drugs. The Registry on Blood Dyscrasias has been set up for the express purpose of alerting the medical profession to the possible toxic effect on blood and bone marrow of drugs or chemical agents. It is not intended to provide statistical information on the incidence of such conditions but to assist physicians in recognizing such possibilities. There may be doubt in some cases as to whether there is a causal relationship between the condition and the use of the substance. The accumulation of a larger number of cases will make it possible to determine with greater certainty whether a causal relationship exists. The untoward side-effect of many of the newer therapeutic agents may not become apparent until the drug has had wide distribution. It is hoped that the registry can serve a useful purpose by alerting physicians and that they, in turn, will report all cases in which they suspect such a possibility. The success of the project will depend therefore on the cooperation of the physicians of the United States. Copies of the summary tabulation and report forms may be had by writing to the Secretary, Committee on Research, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

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[1] Sterilisation by Steam Under Increased Pressure, a Report to the Medical Research Council by the Working Party on Pressure-Steam Sterilisers, Lancet **1**:425-435 (Feb. 28) 1959.

[2] Suggested Recommendations for Prevention and Minimizing the Effects of Hospital Infections, with Special Emphasis on Staphylococcal Infections, Madison, Wisconsin State Board of Health, 1958. Hurst, V.; Grossman, M.; Ingram, F. R.; and Lowe, A. E.: Hospital Laundry and Refuse Chutes as Source of Staphylococci Cross-Infection, J. A. M. A. **167**:1223-1229 (July 5) 1958. Adams, R., and others: Control of Infections Within Hospitals: Special Reference to Prevention Within Operating Rooms, ibid. **169**:1557-1567 (April 4) 1959. Conference on Staphylococcic Infections, ibid. **166**:1177-1203 (March 8) 1958.

ORGANIZATION SECTION

STATEMENT OF DR. LEONARD LARSON ON H. R. 4700, BEFORE WAYS AND MEANS COMMITTEE OF HOUSE OF REPRESENTATIVES

Mr. Chairman and Members of the Committee:

I am Dr. Leonard Larson of Bismarck, North Dakota. I am appearing here today as the Chairman of the Board of Trustees of the American Medical Association. With me is Dr. Frederick C. Swartz of Lansing, Michigan, who is Chairman of the American Medical Association's Committee on Aging.

Dr. Swartz will present the basic reasons for the position of the medical profession concerning H. R. 4700, 86th Congress. Initially, however, I would like to report briefly to the Committee concerning the sustained progress that is being made under the present system of health care in this country.

Slightly more than one year ago, I appeared before this Committee and pledged the American Medical Association to a dedicated, continuing effort in the field of health care for the aged.

I am proud to be able to tell you that the American Medical Association is making good on that pledge.

I say this with humility, because the very real progress being made represents the cooperative effort of hundreds of thousands of our citizens—doctors, nurses, dentists, social workers, hospital staff members, insurance company personnel, community and religious leaders—all working voluntarily together to do the job.

It is also to the credit of these private citizens that they are proving their ability to do the job in their own communities—and to do it effectively and well. A few specifics from their record of accomplishment are appended to our testimony.

At this time it is enough to say that retirement villages, new nursing homes, chronic disease care centers, home care programs, recreational facilities and research projects have been established and that many, many more are on the way.

The medical profession takes pride in the part it has played thus far, and accepts its continuing role of leadership and support in the years ahead with confidence. We believe that the ultimate solution to the problems that remain must be found in private and voluntary action at the community level, and in private health insurance.

Let me say a few words on the subject of voluntary health protection insurance, which has made revolutionary progress since World War II. Yet as rapidly as it has expanded in that period it seems to be gaining momentum still.

At the end of 1945, only 32 million people were covered by voluntary health insurance. But by the end of 1958, the number had soared to 123 million.

Putting it another way, fewer than one American out of three in 1945 had voluntary health insurance. Yet today, the figure is nearly three out of four.

This is important, because it indicates that prepayment plans and the health insurance industry, by providing more and expanded health coverage for all age groups, are anticipating and solving tomorrow's health care financing problem of the aged.

H. R. 4700 fails to take into account the ever-increasing number of persons who will be covered by private health policies when they reach age 65, and the increasing public awareness of the value of voluntary health insurance protection.

Last December, the A. M. A. House of Delegates, aware of medicine's responsibility in this regard, adopted a proposal which applies specifically to those over 65 with modest resources or low family income. This proposal urged physicians to set their fees at a level which will encourage the continued development of insurance and prepayment plans at reduced premiums.

Our state and local medical associations have been moving promptly to make this policy effective.

I am happy to report that there are now 25 plans in 23 states offering Blue Shield programs for those over 65. Further, in sixteen other states, our medical societies, in cooperation with the plans they sponsor, are working out plans of a similar nature.

The progress of Blue Cross and Blue Shield is only part of the story. An ever-increasing number of private insurance companies are now making initial coverage available to those over 65 on an individual basis and, at the same time, improving the type of health insurance coverage provided.

According to the Health Insurance Association of America, 60 per cent of our senior citizens who need and want health insurance will have protection by the end of next year. Further, that percentage will increase until three-quarters will be covered in 1965, and 90 per cent in 1970.

Private insurance and prepayment plans are rapidly doing the job.

But their gains would be nullified by passage of H. R. 4700, which would undermine and gradually replace voluntary health insurance if it were allowed to become law. Few people would be willing or able to carry both government and private plans.

In addition to discussing the progress which has been made in developing financing mechanisms, it should also be remembered that the medical profession has, for many years, intimately concerned itself with the health care of the aged. I believe that the record of medical accomplishment attests to the fact that we have translated this concern into positive action. It should be understood in this connection that medical progress is linked irrevocably with the opportunity of medical researchers and practitioners to work with complete freedom.

Since the beginning of the Twentieth Century, medicine has made revolutionary advances that have lengthened life and opened entirely new approaches to curing illnesses. Since 1900, better medical care has increased the life expectancy of the average American by 20.5 years.

This means that the medical profession itself has helped to swell the ranks of our aged population. We are proud of this, and are convinced that we can meet future challenges in the same way, with the same success and with the same benefits to mankind.

We believe, therefore, that any proposal that would undermine or destroy the voluntary progress we are now making should be defeated. We believe a federal compulsory health care system can lead only to disillusionment and to inferior medical care for those millions of older citizens who deserve the opportunity of making their extra years rewarding.

With your permission, Mr. Chairman, I would like to call on Dr. Swartz to present additional views with respect to H. R. 4700.

We will then be happy to answer any questions that members of the Committee may have.

STATEMENT OF DR. FREDERICK C. SWARTZ ON H. R. 4700, BEFORE WAYS AND MEANS COMMITTEE OF HOUSE OF REPRESENTATIVES

Mr. Chairman and Members of the Committee:

As Dr. Larson has told you, the medical profession is opposed to H. R. 4700, 86th Congress, now pending before this Committee. Before presenting my statement, I should like to thank the Committee on behalf of the American Medical Association for the opportunity to testify.

The fundamental and over-riding reason for the opposition of medicine to this legislation is that it would, in our opinion, result in poorer—not better—health care for the people of this country. The American Medical Association's objective is—and always has been—to work toward the better health of Americans of all ages.

We are for all proper courses of action which will help us attain that objective. We are against any course of action which hinders or prevents its attainment.

As a doctor, it is my daily responsibility to help the aged—to treat them; to help them help themselves. And believe me, gentlemen, one of the best ways to understand the problems of the aged is to serve them as a physician.

It has been my experience that the aged want just about the same things that all the rest of us do: to be part and parcel of their environment; to feel that their skills and talents have value, and can still be used; to be productive; to be loved; to belong.

There is no doubt about it: the problems of the aged are far broader than those of health alone.

Consider, for example, the field of employment, where compulsory retirement policies often undermine the individual's ego, his will to live, his feeling of usefulness.

Able and anxious to work, he frequently finds his abilities no longer in demand. Unnecessarily placed on the shelf, he feels as if he has been cashiered out of the human army without rank, weapons, medals, or identification.

The public fails to realize that the older citizen continues to have many special needs—In the field of housing; in recreation; in finding acceptance and understanding within the community. He also needs preparation in advance, if his added years of life are to be full and rewarding.

These are not health problems, but they bear on health. And until society recognizes this, it will continue to consider in a piecemeal, hit-or-miss way a problem that requires a broad, total approach.

Concern for these problems animates all thoughtful people.

I can assure you that the doctors of the country are concerned.

For they know, as well as any group, that behind the array of statistics are individual men and women —that while each human being is alike, each is also very different.

And so when physicians hear broad statements about the problems of the aged, when they are asked to consider the across-the-board solutions that are proposed, they tend to apply the acid test of personal experience.

Would these proposed solutions really work? Would they really help the people whom the doctor serves, the individual patients whose problems and needs he knows so intimately?

It is by this yardstick that the physician measures his reply. And it is by this yardstick that the members of the medical profession have formulated their position with respect to H. R. 4700 and similar bills.

I would like to discuss some of the fundamental reasons why we believe that this proposed legislation is neither practical nor realistic.

Medical care is not susceptible to production-line techniques.

Care for any segment of our population—the aged included—calls for a cooperative attack on the problem by nurses, doctors, hospitals, social workers, insurance companies, community leaders and others. It requires flexibility of medical technique—an ingredient which would unquestionably vanish the moment government establishes a health program from a blueprint calling for mass treatment.

If we abandon the community approach in favor of a rigid national health program we will, in effect, have constructed another Procrustes' bed. The mythological Procrustes, you will remember, developed a bed that was just the right size for everybody. There was only one trouble with it:

Procrustes, instead of altering the bed to fit the person, altered the person to fit the bed.

He accomplished this feat of legerdemain by trimming off the legs of the tall, and stretching his shorter victims on the rack.

I am sure we all agree that it is sounder to tailor the bed to fit the patient.

In the case of the aged, their health problem primarily involves acute illness and the so-called degenerative diseases. In a very large percentage of cases, the main need is not for an expensive hospital stay or a surgical operation, but for medical care at home or in the doctor's office. In other cases, the important requirement is nursing care in the patient's home, or the home of relatives. And in still others, custodial care in a nursing home or public facility may be the only answer. The point is that the medical needs of this particular segment of the aged are subject to countless variations. Any workable system of care must be tailored to meet these variations. An example of a faulty program is the mass attack approach that has been forced on medicine in the handling of the mentally afflicted. They are removed from society but their medical problems have not been solved.

If H. R. 4700 were enacted, it would mean that the Federal government would finance the health care of OASDI beneficiaries through compulsory and earmarked taxes; the Federal government would control disbursement of funds; the Federal government would determine the benefits to be provided; the Federal government would set the rates of compensation for hospitals, nursing homes, dentists, and physicians; the Federal government would audit and control the records of hospitals, nursing homes and patients; and the Federal government would promulgate and enforce standards of hospital and medical care.

When government at any level guarantees services which it cannot itself provide, it inevitably tends to control the purveyors of those services. I doubt that anyone here intends or seeks such control, but there is no doubt that it would take place.

Disclaimers notwithstanding, if a single government agency were to buy 10 to 20 per cent of all care in the nation's general hospitals, it would be utterly impossible to limit that agency's power to influence the over-all operation and management of hospitals.

One predictable consequence of such a national program would be the overuse and overcrowding of our hospital facilities. It is certain that a substantial increase in hospital use would result during the first year of this proposed program—simply because a government plan had been put into operation.

As doctors, we believe that patients should be placed in hospitals, nursing homes and other institutions only when necessary. We believe the length of their stay, as well as the therapy rendered, should be dictated only by their medical condition and not by limitations of legislation or regulations.

The problem is far more than a matter of economics, or even of medical technique. For we must also deal with the human spirit, which flourishes best in those who are determined to stay in the mainstream of day-to-day living.

H. R. 4700 would have further bad effects.

—It would curb community incentive to support hospitals, for the tendency would be to shift this responsibility from the shoulders of private and local governmental sources to the already overburdened shoulders of the Federal government.

—It would discourage, at the community level, the freedom to experiment with new techniques, such as home care programs, day hospital service, homemaker services, progressive patient care, and new concepts for treatment through outpatient departments and doctors' offices. And it is at the community level that such innovations are developed and made to work.

—It would discourage families from taking care of their own.

—It would restrict beneficiaries in their choice of hospital and physician. For only those physicians, and those hospitals and nursing homes entering into agreements with the Federal government, would participate.

—The professional relationship between the doctor and his patient—the basis of all effective health care—would be severely handicapped. Government regulation would be imposed on the physician, and on the patient as well, bringing a third and intruding party between them. Required conformance to administrative regulations could also hamper the physician from prescribing treatment which, in his professional opinion, was indicated.

—It would discourage the individual approach to patient care. When this has been disregarded in the past, the result has been mass tragedy rather than mass cure.

—It would attempt to chart a health program for the aged without accurate knowledge of the problem's dimensions. The statistics presently available on the subject are neither conclusive nor complete.

To use them as the basis for so far-reaching a program is akin to prescribing for the patient without first making a diagnosis.

Basically, H. R. 4700 simply proposes a form of national compulsory health insurance. For the moment, it would be limited in scope; however, there are many who are testifying before this Committee this week who admittedly seek to extend the program to every segment of the population. It should be remembered in this connection that, if the Federal government at some future date adopts a medical care program for the total population, it will be assuming a medical bill of more than $20 billion annually. A report published by the Department of Health, Education and Welfare, based on 1957 statistics, indicates that private health care costs approximate $15 billion and that public and philanthropic costs amount to about $5 billion annually.

The bill would establish a dangerous precedent. Instead of cash benefits, it proposes service benefits irrespective of need. In effect, the Federal government would furnish the beneficiary with compulsory hospital and surgical insurance whether he needed it or not, whether he wanted it or not.

In this connection, let me say that the A. M. A. has never opposed the Social Security Act per se. H. R. 4700 is, however, a major and dangerous deviation from the original concept of the system.

We must also face the fact that any single program of health care for the aged should not embrace every aged person. The pending bill would cover millions of people who do not need or want government medicine.

Further, it is a misconception to think that this measure would aid those who receive Public Assistance, the vast majority of whom are not covered by Social Security. These indigent are now receiving their medical care through welfare programs. Aside from the help they get from many private, fraternal and religious organizations, the indigent now receive more than $4 billion annually in federal and state aid for medical and other expenses.

I should like to comment briefly on what this proposed legislation would cost.

It would be staggeringly expensive.

The costs of this program during its first and second years have been estimated as in excess of $2 billion a year, a figure which can be expected to increase during the ensuing years.

There is absolutely no way of predicting the cost of H. R. 4700 in the years ahead. These programs expand. They never contract. And once they are on the books, they are there to stay.

Yet the problem of financing health services for the aged is a temporary, not a permanent one. As Dr. Larson indicated, voluntary health insurance is making tremendous progress, through expanded coverage and broader protection.

Dozens of different type policies are now available. Among them are policies guaranteed renewable for life; policies to cover those now over 65; coverages that will continue after retirement; and group policies that may be converted to individual coverage upon termination of employment.

Much of this progress has been made in just a few years. This indicates that the hospital costs of our aged are being met, in a large measure, by prepayment plans and insurance, as they steadily gain experience in this relatively new field of coverage.

Much progress is also being made in the development of new and improved facilities specially tailored to the particular health requirements of the older citizen.

As a part of this program, the A. M. A. has supported a loan program of the F. H. A. type for non-governmental hospitals and nursing homes, whether of a non-profit or proprietary nature. It has also recommended changes in the Hill-Burton Act to help the individual states earmark more money for non-profit nursing homes.

The A. M. A. continues to back further experiments in progressive hospital care; home care programs; and homemaker services, all of which have the common purpose of improving the quality of medical care by reducing the length of hospital and nursing home confinement through the earlier discharge of patients.

The record shows that sustained and heartening progress is being made throughout the United States toward meeting the needs of our older citizens promptly and positively.

I do not have the time to specify here the details of the massive job that is being done. The fact is that voluntary methods—supported by the cooperative effort of many thousands of our citizens—are meeting the challenge and will continue to meet the challenge, given the continued opportunity.

So that this Committee has at its disposal the American Medical Association's six-point program for older citizens, we are appending a discussion of that program which I had the privilege of giving last month before the U. S. Senate Sub-committee on the Problems of the Aged and Aging.

In closing, one fact seems to me to be crystal clear:

The health professions and other private voluntary groups are meeting the challenge. We believe that the same people who made this the healthiest nation in the world's history, and helped bring the gift of longer life to millions of Americans, are equipped to meet the problem of caring for the health of our older citizens.

Gentlemen, this concludes my formal statement. It is our sincere recommendation that H. R. 4700, 86th Congress, not be favorably considered by this Committee.

Dr. Larson and I will be glad to answer any questions you may have.

LETTER ON AIR POLLUTION

June 26, 1959

Kenneth A. Roberts, Chairman
Health and Safety Subcommittee
Interstate and Foreign Commerce Committee
House of Representatives
Washington 25, D. C.

Dear Mr. Chairman:

I should like to take this opportunity on behalf of the American Medical Association to respectfully submit for your consideration our views on H. R. 2347 and S. 441, 86th Congress, which we understand are now pending before your Committee.

It is our understanding that these bills would extend the duration of the Air Pollution Control Act beyond June 30, 1960. H. R. 2347 would extend the law until June 30, 1965, whereas S. 441 would extend the law until June 30, 1964.

Before commenting on the specific bills, I should like to refer to the general subject of air pollution briefly, which has been defined by our Council on Industrial Health as an excessive atmospheric concentration of foreign matter that may adversely affect the well-being of a person or cause damage to property. Although a health hazard need not be demonstrated to establish the need for the control of air pollution, our interest in this subject is mainly with respect to the relationship of air pollution to health.

Although a number of scientific investigations of air pollution have recently been completed and others are currently being conducted, there are special limitations which make this type of investigation unusually difficult. Experimental studies of the health effects of these pollutants, singly and in combinations, must be conducted in exposure chambers in the laboratory to evaluate the synergistic effects they have upon one another. Observations must be made of the effects on the health of workers in industry exposed to various substances which pollute the air of their work place and which may pollute the air of the surrounding community. However, most productive are epidemiologic and clinical studies of the effects upon the health of the population of a community produced by pollutants in the atmosphere, existing as they do in combinations and affected as they are by sunlight and atmospheric conditions.

It is apparent that future research on the subject of air pollution and its relation to health is highly desirable. We believe that the Air Pollution Control Act which was enacted in 1955 represents a proper approach to the problem. The philosophy of the Act recognizes the primary responsibility of state and local governments in controlling air pollution. Within the framework of a coordinated national program, established under the direction of the Surgeon-General of the United States Public Health Service, we believe there is sufficient flexibility to stimulate the initiative of local agencies and to permit states and communities to deal with the phases of the air pollution problem most important to them. Although the interest of the federal government in the subject of air pollution may not be a permanent one, we feel that sufficient federal responsibility can still be demonstrated to justify the appropriation of limited federal funds in support of research activities in this field for an additional period of time.

The American Medical Association, therefore, recommends that your Committee give favorable consideration to H. R. 2347 and S. 441, 86th Congress. I respectfully request that the foregoing comments on behalf of the American Medical Association be included in and made part of the record of hearings on these bills.

Sincerely yours,
F. J. L. Blasingame, M.D.
Executive Vice-President

NATIONAL MEETING ON MEDICAL ASPECTS OF SPORTS

A National Conference on the Medical Aspects of Sports is being planned to immediately precede the clinical sessions of the American Medical Association at Dallas, Texas, Nov. 30, 1959. The Conference, to be held under the auspices of the A. M. A.'s Committee on the Medical Aspects of Sports (formerly the Committee on Injury in Sports) will be open to athletic directors, coaches, and trainers as well as interested physicians.

The program, to include a wide variety of subjects relating to the health aspects of athletics, will cover the general areas of the physiology and pharmacology of exercise, the training and conditioning of the athlete, and the prevention and treatment of injuries.

Papers to be presented include "Amphetamine Sulfate and Athletic Performance, II Subjective Responses," "A Medical Program for High School Football," "Exercise and the Oxygen Debt," "The Biodynamic Potential of the American Male," "Exercise and the Kidney," "The Pathology of Trauma," and many other subjects to be announced later. Two panels, one covering "The On-Field Responsibilities of the Team Physician" and the other dealing with "The Prevention of Head Injury in the Athlete" are scheduled.

The date and place of the conference (Nov. 30, 1959, in Dallas) were selected so that physicians could conveniently combine attendance with participation in the A. M. A. clinical sessions. Those who wish to receive future announcements concerning the conference may address the Committee on the Medical Aspects of Sports at the A. M. A. offices in Chicago.

Postgraduate Courses for Physicians

Compiled by the Council on Medical Education and Hospitals for the Period Sept. 1, 1959, to Aug. 31, 1960[1]

The data in the following list of postgraduate courses have been compiled by the staff under the supervision of Dr. Glen R. Shepherd, Assistant Secretary of the Council on Medical Education and Hospitals. The Council desires to express appreciation to the officers of the medical schools, hospitals, and medical societies who have cooperated in furnishing the information essential to the preparation of this report.

Walter S. Wiggins, M.D., Secretary
Council on Medical Education and Hospitals

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INTRODUCTION

The fifth annual listing of postgraduate courses in this country for physicians appears in the following pages of The Journal. This listing is for the period Sept. 1, 1959, to Aug. 31, 1960. The annual list replaces the semiannual lists that appeared previously.

The purpose of the single annual listing is to bring together in one place information secured about postgraduate courses to be offered in the year ahead. It is the consensus that such a single annual listing provides a reference that potential physician-enrollees are more likely to consult than do single notices in random issues of The Journal. Further, such a list encourages long-range advance planning of the courses that in the opinion of the Council and other medical educators is likely to contribute significantly to improvement in the quality of the courses so planned. The general acceptance of a single annual listing will make possible the publication of a selective listing of the more educationally meritorious programs when a suitable appraisal mechanism has been thoroughly tested. Such studies are now under way. Therefore, it is expected that supplementary notices of postgraduate courses will not be published in The Journal.

Postgraduate medical education courses consist of planned activities for doctors of medicine intended to refresh practicing physicians in the various aspects of their basic medical education, to provide information on new developments in medicine, and to stimulate further educational efforts by the participants. Such courses are not designed to provide the lengthy intensive education required for initial training for a specialty. This is graduate medical education, usually comprising residency training or fellowships. Postgraduate courses are shorter than graduate education programs.

This list of postgraduate courses was prepared from the unappraised and unevaluated replies to Council questionnaires by American medical schools, hospitals, and the various national, state, and specialty medical societies. This list is printed simply to provide for those physicians seeking postgraduate courses a point of departure through which further information can be obtained by writing to the institution or organization listed under Location. Inquiries should be made before traveling to any course listed, because dates, time arrangements, and fees are subject to change. Sponsors of courses having numerical limitation of registration must restrict enrollment, often on the basis of order of application. Courses for which there is insufficient advance registration may be canceled. Such inquiry of the sponsor is especially urged about courses scheduled for 1960, on which final information may not have been available to the sponsor at the time this list was prepared.

Though the educational values of medical society meetings and conventions as well as hospital staff and departmental meetings can be very real and worthwhile, such meetings are not usually listed here as postgraduate courses. Lists of meetings are to be found periodically elsewhere in The Journal.

Many of the courses have co-sponsors to whom specific credit cannot be given because of space limitations. It is expected that the institution or organization sponsoring the course has provided such co-sponsor recognition to its registrants.

Under each category in the following list, the order of arrangement of the courses is alphabetically, first by states, second by cities within state, third by the institutions and organizations within the cities, and last by date of course where several courses in that category are offered by the same institution or organization.

Although the list may indicate that a course is designed primarily for specialists in that category, many such courses are open to any physician, so specific inquiry should be made of the institution listed.

One of the categories has a special use in addition to its usual denotation. In the General Medicine category are listed those courses having subjects embracing several fields, such as a course on the management of mass casualties or the Summer School of Alcohol Studies.

Following the list of courses appears a geographical cross-reference alphabetically by state and city of the categories under which courses so located are listed. This should assist doctors seeking courses in a certain location to find their listing.

KEY

Designed For

G—General practitioners
S—Specialists
B—Both
Lim—Enrollment limited to specified number with number stated; i. e., Lim 20, meaning enrollment limited to 20 in the course. If it is repeated, another 20 could be accommodated

Type

IC—Intensive continuous
II—Intensive intermittent
CC—Circuit course
PT—*Postgraduate traineeship**
HS—Home study
HS (C)—Home study by correspondence
HS (R)—Home study by radio
O—Other

Time Arrangement

C—Continuous or concentrated (e. g., as every day for five days)
I—Intermittent (e. g., every Thursday for six weeks)

Methods of Education

AV—Audiovisual aids (movies, slides, models)
BR—Bedside rounds
Clin C—Clinical conference
Dem—Demonstrations other than of patients
EPP—Enrolee performs procedure
LC—Live clinic
Lab—Laboratory work (including cadaver dissection and dog surgery where applicable)
Lec—Lecture
O—Open question periods
PD—Patient demonstration
Pan—Panel discussion
PT—Postgraduate traineeship*
R—Radio or telephone
Sem—Seminar
Surg—Operative human surgery
TV—Television

*A postgraduate traineeship *for practicing physicians* is an individually arranged residency-type postgraduate educational experience in a hospital usually with residents in that field. It differs from a residency or fellowship in the following ways: 1. It is not primarily intended to provide training for entering specialty practice or, in itself, to qualify for specialty board certification. 2. Therefore, it is of shorter duration than a year. 3. It usually does not provide either a stipend or housing, and it may exact a fee from the physicians in such training. 4. It may not (or may) involve direct patient responsibility.

ALLERGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Graduate Instructional Course in Allergy	Dr. John D. Gillaspie, Treasurer American College of Allergists 2019 Broadway, Boulder, Colo.: course at Americana Hotel, Miami Beach, Fla.	G	IC	Lec, Pan, O, AV	20	2/28/60	3/ 1/60	C; 3 days	50, 3 days; 35, 2 days; 20, 1 day; for non-members; members, 15 total
Postgraduate Course in Hypersensitivity—Part I	Children's Hospital 2125 13th St., N.W., Washington, D.C.	G Lim 100	IC	Lec, O, AV	12	11/21/59	11/22/59	C; 2 days	35
Postgraduate Course in Clinical Hypersensitivity—Part II	Children's Hospital 2125 13th St., N.W., Washington, D. C.	G Lim 100	II	PD, LC, Lec, O, AV	12	1/ 5/60	2/ 9/60	I; 6 sessions 2 hr. weekly, Tuesdays	35
Personal Course in Allergy	*Cook County Graduate School of Medicine* 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Lec, O, EPP	500	Arranged	6 mo. later	6 mo. full time	500
Allergy	Tufts University School of Medicine 136 Harrison Ave., Boston; course at New England Center Hospital 171 Harrison Ave., Boston	G Lim 100	IC	PD, LC, Clin C, Lec, Pan, O, EPP	18	3/ 3/60	3/ 5/60	C; 2½ days	30
Allergic Diseases	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 40	IC	PD, LC, Clin C, Lec, O, AV	18	3/17/60	3/19/60	C; 3 days	40
Allergy and Immunity in Pediatrics	Hansel Foundation 634 N. Grand Blvd., St. Louis; course at Park Plaza Hotel, St. Louis	S Lim 50	IC	Lab, Lec, Pan, O	35	5/25/60	5/29/60	C; 5 days	150
Medicine PM 68	Columbia University College of Physicians and Surgeons. 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 10	II	LC, Lec, O, AV	28	9/10/59	12/17/59	I; 14 sessions 2 hr. weekly, Thursdays	50
Pediatric Allergy	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., *and 106th* St., New York	S Lim 12	II	LC, Clin C, Sem, Lec, O	180	11/ 4/59	5/25/60	Wednesdays	300
Allergy in Theory and Practice	Roosevelt Hospital, The Institute of Allergy 128 W. 59th St., New York 19	B Lim 25	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	10	5/16/60	5/21/60	C; 5½ days	100
Clinical Allergy—Office Management	Montefiore Hospital 5th Ave., Pittsburgh	G Lim 3	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	3 mo.	4/60	7/60	3 mo. Full time	250
Clinical Allergy—Practical Considerations in Management	Montefiore Hospital 5th Ave., Pittsburgh	G Lim 50	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	10	4/18/60	4/23/60	C; 5 days	65
Allergy	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at Texas Medical Center Houston, Tex.	S	IC	Lec, AV	24	2/60	2/60	C; 4 days	50

ANATOMY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Gross and Applied Anatomy	San Diego County General Hospital North end of Front St., San Diego 3, Calif.	S Lim 20	II	Lab, Lec, O, AV	32	9/59	12/59	I; 16 sessions 2 hr. weekly, Wednesdays	Nil

Surgical Anatomy	St. Mary's Hospital 2200 Hayes St., San Francisco	S Lim 100	II	Lab, PD, Clin C, Lec, O	30	9/ 1/59	7/ 1/60	I; 20 sessions 1½ hr. twice monthly, Fridays	NB
Surgical Anatomy	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	Lab, Lec	150 or more	3/21/60	6/60	C; 3 hr. week lec. and dem. 12 hr. week dissection	20
Anatomy 201—Special Dissections in Anatomy	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	II	Lab, EPP	Arranged	Arranged		Arranged	Arranged
Anatomy 202—Demonstrations in Anatomy	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	II	Lab, O, AV	50	9/59	5/60	I; 30 sessions Arranged	175
Applied Anatomy	Mercy Hospital, Inc. Calvert and Saratoga Sts., Baltimore 2	B	II or PT	Lab, PD, Lec, O, AV		9/59	5/60		Unknown
General Anatomy	Postgraduate Committee, University of Maryland School of Medicine 522 W. Lombard St., Baltimore	S Lim 3	II	Lab, Lec, Pan	Arranged	Arranged		Arranged	Arranged
Clinical Anatomy	Postgraduate Committee, University of Maryland School of Medicine 522 W. Lombard St., Baltimore	S Lim 20	II	Lab, Lec	90	1/25/60	5/25/60	I; 30 days 3 hr. twice weekly, Mondays, Wednesdays	150
Surgical Anatomy	Harvard Medical School 25 Shattuck St., Boston	S Lim 16	IC	Lab, Lec	140	3/ 7/60	4/29/60	C; 40 days	225
Anatomy	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Lim 50	II	Lab, Lec, O	60	2/11/60	5/26/60	I; weekly on Thursday	65
Anatomy (Surgery)	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Surg. Lim 10	IC or PT	Lab, Lec, O	240	4/11/60	6/ 3/60	C; 40 days	100
Anatomy (Obstetrics and Gynecology)	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Lim 10	PT	Lab, Lec, O	90	4/11/60	4/30/60	C; 15 days	65
Surgical Anatomy Review	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 17	II	Lab, Surg, O, AV, EPP	54	1/60		I; 18 sessions 3 hr. weekly, Mondays	250
Surgical Anatomy—Dissection of Upper Extremity	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, O, EPP	24½	9/15/59	10/27/59	I; 7 sessions 3½ hr. weekly, Tuesdays	125
Surgical Anatomy—Dissection of *Head and Neck*	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, O	31½	11/ 3/59	1/12/60	I; 9 sessions 3½ hr. weekly, Tuesdays	150
Surgical Anatomy—Dissection of Thorax	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, O	10½	1/19/60	2/ 2/60	I; 3 sessions 3½ hr. weekly, Tuesdays	50
Surgical Anatomy—Dissection of Abdomen	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, O	21	2/ 9/60	3/15/60	I; 6 sessions 3½ hr. weekly, Tuesdays	100
Surgical Anatomy—Dissection of Lower Extremity	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	**Lab**, Sem, O	17½	3/22/60	4/19/60	I; 5 sessions 3½ hr. weekly, Tuesdays	75
Surgical Anatomy	Cornell University Medical College 1300 York Ave., New York 21	S Lim 25	IC	Lab, Lec, O, AV, EPP	180	5/23/60	6/18/60	C; Unknown	200
Gross Anatomy on Cadaver for Anesthesiologists	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	IC	Lab, O, EPP	240	2/ 8/60	4/ 1/60	C; 40 days	300
Gross Human Anatomy on Cadaver for Roetgenologists	New York Medical College Flower and Fifth Ave. Hospitals *Fifth Ave., and 106th St., New York*	S Lim 10	IC	Lab, O, EPP	240	2/ 8/60	4/ 1/60	C; 40 days	300
Review of Gross Human Anatomy on Cadaver for Surgeons	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	IC	Lab, O, EPP	240	2/ 8/60	4/ 1/60	C; 40 days	300
Gross Human Anatomy on Cadaver for Otolaryngologists	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	IC	Lab, O, EPP	90	2/ 8/60	2/29/60	C; 15 days	125
Gross Human Anatomy on Cadaver for Orthopedists	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	IC	Lab, O, EPP	84	2/23/60	3/11/60	C; 14 days	75
Gross Human Anatomy on Cadaver for Obstetricians and Gynecologists	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	IC	Lab, O, EPP	84	3/15/60	4/ 1/60	C; 14 days	75
Anatomy on Cadaver for Urologists	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	IC	Lab, O, EPP	84	3/15/60	4/ 1/60	C; 14 days	75

Key will be found on page 1938.

ANATOMY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Anatomy-Surgical by Cadaver Demonstration	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	II	Lec, O, AV, EPP	18	Arranged		I; 6 sessions 3 hr. Mondays, Wednesdays	300
2411-Surgical Anatomy of the Head and Neck	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/21/59	12/11/59	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
2412—Surgical Anatomy of the Thorax and Its Viscera	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/21/59	12/11/59	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
2413—Surgical Anatomy of the Abdomen	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/21/59	12/11/59	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
2583—Anatomy for Orthopedic Surgeons	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	Lab, O, EPP	35	1/11/60	1/15/60	C; 5 days	165
2414—Surgical Anatomy of the Female Pelvis	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	3/21/60	6/10/60	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
2415—Surgical Anatomy of the Genitourinary System	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	3/21/60	6/10/60	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
2416—Surgical Anatomy of the Musculoskeletal System	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	3/21/60	6/10/60	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
Regional Anatomy	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Texas	G Lim 12	II	Surg, Lec, EPP	80	9/ 3/59	6/60	I; 40 sessions 2 hr. weekly, Thursdays	100
ANESTHESIOLOGY (See also Anatomy)									
Anesthesiology in General Practice	Lloyd Noland Hospital and Clinic P.O. Box 538, Fairfield, Ala.	G Lim 3	IC or II or PT	PD, LC, BR, Clin C, Surg, Lec, Pan, O, AV, EPP	6 hr. daily Full time with night call	Arranged Arranged		30 to 90 days	Varies Varies
Anesthesiology	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	1125	Arranged every 3 mo.	At least 3 mo. later		350
Course I—Regional Anesthesia	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 1	IC	Lab, PD, LC, Sem, Surg, Lec, O, EPP	140	1st Monday each mo.	Friday of 4th wk.	C; 20 days	300
Course V—Inhalation and Endotracheal Anesthesia	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 1	IC	Lab, PD, LC, Sem, Surg, Lec, O, EPP	140	1st Monday each mo.	Friday of 4th wk.	C; 20 days	300
Medical Traineeship in Anesthesiology	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	PT	PD, LC, BR, Clin C, Sem, Lec, O	160	Arranged	3 weeks later	Arranged	150
Anesthesia for General Practitioners and Part-time Anesthesiologists	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	14	4/ 6/60	4/ 7/60	C; 2 days	25
Clinical Traineeship in Anesthesiology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	BR, Clin C, Sem, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. nonresidents
Anesthesiology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	Lec, Pan, O, AV	21	4/11/60	4/13/60	C; 3 days	45
Anesthesia	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 50	IC	Clin C, Sem, Lec, Pan	20	3/10/60	3/12/60	C; 2½ days	25
Postgraduate Lectures in Anesthesiology—Basic Science and Clinical	Maine Medical Center 22 Bramhall St., Portland, Me.	G	II	Sem, Lec, O, AV	15	10/16/59	5/60	I; 15 sessions 1 hr. twice monthly, Fridays	Nil
Regional Anesthesia	University of Missouri School of Medicine 807 Stadium Rd., Columbia, Mo.	G Lim 15	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP	30	Arranged		C; 5 days	100
One Day Postgraduate Seminar in Anesthesiology	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark 2, N. J.; course at Cherry Hill Inn, Dover Township, N. J.	S Lim 40	IC	Sem, Lec, Pan, O, AV	8	3/26/60	3/26/60	C; 1 day	Unknown

Anesthesia	University of Buffalo School of Medicine 3435 Main St., Buffalo	G Lim 12	IC	PD, Sem, Lec, Pan, O, AV	39	4/ 4/60	4/ 9/60	C; 5½ days	75
Anesthesia and Analgesia in Obstetrics	New York Medical College Metropolitan Medical Center Fifth Ave. at 106th St., New York 29	G	IC	PD, Sem, Lec, AV, EPP	15	Arranged		C; 5 days	125
Anesthesiology—Special Techniques in Anesthesia	New York Medical College Metropolitan Medical Center Fifth Ave. at 106th St., New York 29	G	IC	PD, Sem, Lec, AV, EPP	15	Arranged		C; 5 days	125
Endo-Tracheal Techniques in Anesthesia	New York Medical College Metropolitan Medical Center Fifth Ave. at 106th St., New York 29	G	IC	PD, Sem, Lec, AV, EPP	15	Arranged		C; 5 days	125
Applied Anesthesiology	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, BR, Lec, O, AV	480	4/ 1/60 10/ 1/60	6/30/60	C; 72 days	300
Postgraduate Training in Anesthesia for the Part-time Anesthetist	New York State Society of Anesthesiologists 131 W. 11th St., New York 11; course at various hospitals throughout New York State	G	O	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec, EPP	Variable	Arranged		Variable	Nil
#512-Anesthesiology (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 3	II	PD, Clin C, Surg, Lec, EPP	70	9/59	9/60	I; 10 days, any Monday	175
#513-Regional Anesthesiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 16	IC	Lab, PD, Lec	42	9/14/59 1/11/60	9/19/59	C; 6 days	135
#511-Anesthesiology: Endotracheal and Related Methods	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 4	IC	Lab, PD, Clin C, Surg, Lec, EPP	35	9/28/59 1/25/60 3/21/60	10/ 3/59	C; 5 days	135
Inhalation Anesthesia	McKesson Anesthesia Associates 2228 Ashland Ave., Toledo, Ohio; course at various Toledo Hospitals	G Lim 2	IC	PD, Clin C, Sem, Surg, Lec, O, EPP	140	Arranged		C; 25 days	250
Recent Advances in the Physiological Aspects of Anesthesia	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 125	IC	Sem, Lec, Pan, O	Unknown	2/ 8/60	2/10/60	C; 3 days	75
Anesthesia Refresher Course	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at Scott and White Memorial Hospital, Temple, Tex.	G Lim 2	IC	PD, BR, Sem, Surg, Lec, O, EPP	176	9/ 7/59	10/ 3/59	C; 24 days	25
Fifth Annual Course in Anesthesiology-Principles and Application	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.	B Lim 270	IC	Lec, Pan, O, AV, TV	20	3/ 9/60	3/11/60	C; 3 days	45
Postgraduate Refresher Course in Anesthesiology	University of Texas Postgraduate School of Medicine 213 W. Avenue G, Temple, Tex.; course at Scott and White Memorial Hospital; Scott, Sherwood and Brindley Foundation, Temple, Tex.	G Lim 1	IC	PD, BR, Sem, Surg, Lec, EPP	176	First Monday in each mo.	Last Saturday in each mo.	C; 24 days	25

BASIC SCIENCES
(See also Clinical Pathology)

Correlation of Medical Basic Sciences	St. Mary's Hospital 2200 *Hayes St., San Francisco*	G Lim 400	II	Clin C, Lec, O	20	9/ 1/59	7/ 1/60	I; 20 sessions 1 hr. twice monthly, Saturdays	Nil
Principles and Techniques of Tissue Culture	Dr. Mary S. Parshley Columbia University, College of Physicians and Surgeons 630 W. 168th St., New York 32; course at University of Colorado Medical School, Denver	Medical Research Personnel Lim 30 (15 active partic.)	IC	Lab, Sem, Lec, EPP	114	Summer 1960		C; 26 days	100
4th Annual Conference on Quantitative Studies of the Growth and Genetic Processes in Mammalian Cells	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20; course at Stanley Hotel, Estes Park, Colorado.	S Lim 50	IC	Sem, Lec, O, AV	32	8/31/59	9/ 3/59	C; 4 days	5
Microbiology 210—Diagnostic Medical Mycology	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	IC	Lab, Sem, O, EPP	150	Arranged		C; 25 days	100
Orthopedic Basic Science	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 16	IC	Lab, PD, LC, BR, Clin C, Sem, Lec	750	7/ 1/60	12/31/60	C; 120 days	600

Key will be found on page 1938.

BASIC SCIENCES—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship in Microbiology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	Lab, BR, Clin C, Sem, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. nonresidents
Histochemistry	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S Lim 18 1st. wk. Lim 24 2nd. wk.	IC	Lab, Sem, Lec, O, AV	84	6/ 6/60	6/18/60	C; 12 days	75 one week; 150 two weeks
Basic Sciences As They Apply to The Practice of Medicine	Postgraduate Committee, University of Maryland School of Medicine 522 W. Lombard St., Baltimore	B Lim 100	II	Unknown	12	1/ 6/60	5/26/60	I; 21 sessions 2 hr. weekly, Wednesdays	50
Modern Research Methods in Biology and Medicine	Director of the Summer Session Massachusetts Institute of Technology Cambridge 39, Mass.	S	IC	Lab, Lec, AV	50	July or August/60		C; 10 days	Not yet determined
Basic Sciences with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	Residents of Affiliated Hospitals; Open to Practitioners B Lim 40	PT	Lab, PD, LC, Clin C, Lec, O, AV		9/28/59	6/ 4/60	8 mo.	500
Bacteriology with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	B Lim 40	IC or PT	Lab, PD, Clin C, Lec, O, AV	60	1/ 4/60	1/16/60	C; 10 days	50
Biophysics with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	B Lim 40	IC or PT	Lab, Clin C, Lec, O, AV	60	1/18/60	1/30/60	C; 10 days	50
Biochemistry with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	B Lim 40	IC or PT	Lab, PD, Clin C, Lec, O, AV	90	2/15/60	3/ 5/60	C; 15 days	75
Physiology with Clinical Correlation	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	B Lim 40	IC or PT	Lab, PD, Clin C, Lec, O, AV	60	3/ 7/60	3/19/60	C; 10 days	50
Pharmacology with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	B Lim 40	IC or PT	Lab, PD, Clin C, Lec, Pan, O, AV	60	3/21/60 3/26/60	4/ 4/60	C; 10 days	50
Biochemistry	Department of Postgraduate Medical Education, Seton Hall College of Medicine 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 40	II	Lec, O, AV	15	Fall/59		I; 10 sessions 1½ hr. weekly, Wednesdays	50
Physiology PM 33—Seminar in Selected Topics in Gastrointestinal Physiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	II	Sem, Lec, O, AV	70	10/ 1/59	6/ 1/60	I; 70 sessions 1 hr. twice weekly, Mondays, Fridays	100
Physiology PM 32—Normal and Pathological Physiology	Columbia University College of Physicians and Surgeons 630 W. 168 St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Lec, O, AV	52	10/ 7/59	4/13/60	I; 26 sessions 2 hr. weekly, Wednesdays	150
Sensory Physiology—Physiology of the Senses With Emphasis Upon Receptors	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 10	II	Lab, Dem, Lec	10	Arranged		I; 10 sessions 1 hr. weekly, Wednesdays	100
Physiology of Reproduction	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 20	II	Sem, Lec	12	Arranged		I; 6 sessions 2 hr. ea.	75
Physiology of the Endocrine System—Survey of Recent Advances With Respect to Basic Concepts	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G Lim 10	II	Lab, Lec, AV	16	9/14/59	11/14/59	I; 8 sessions 2 hr. weekly, Mondays	75
Review of Embryology—Practical Considerations in Developmental Anomalies	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G Lim 15	IC or II	Lec, AV	15	2/ 4/60	4/ 7/60	C; or 1½ hr. Intermittent by arrangement	100
Basic Sciences in Medicine and Surgery	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 15	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	30	4/ 1/60 10/ 1/60	4/ 6/60	C; 5 days	50
2012—Neuroanatomy and Neurophysiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	II	Lab, Lec	120	9/14/59		I; 36 sessions 3½ hr. thrice weekly, Mondays, Wednesdays, Fridays	375

‡1814—Radiochemical Analysis	New York University Post-Graduate Medical Medical School 550 First Ave., New York 16	G	IC	Lab, Lec, AV	70	11/ 9/59	11/20/59	C; 10 days	100
‡161—Clinical Physiology: The Application of Basic Physiology to Diagnostic and Therapeutic Problems	New York University Post-Graduate Medical Medical School 550 First Ave., New York 16	G Lim 35	II	Clin C, Sem, Lec, O, AV	16	3/ 3/60	4/21/60	I; 8 sessions 2 hr. weekly, Thursdays	60
Human Tumor Transplantation—Heterologous Transplantation of Human Tissues	Sloan Kettering Institute for Cancer Research 410 E. 68th St., New York	M.D.'s and senior research investigators Lim 30	IC	Lab, Sem, Lec, Pan, O, EPP	27	10/ 6/59 3/ 8/60	10/ 9/59	C; 3 days	Nil

CARDIOVASCULAR DISEASE

(See also Chest Disease, Electrocardiography, Internal Medicine)

Twenty-Ninth Annual Professional *Symposium*	Los Angeles County Heart Association 660 S. Western Ave., Los Angeles 5; course at Beverly Hilton Hotel, Beverly Hills, Calif.	G	IC	Sem, Lec, Pan, O, AV	16	10/ 7/59	10/ 8/59	C; 2 days	Unknown
‡873—Cardiac Resuscitation	University of Southern California School of *Medicine Postgraduate* Division 2025 Zonal Ave., Los Angeles 33	G Lim 5	II	Lab, Lec, EPP	2	continuous weekly		I; 1 session 2 hr. weekly, Wednesdays	30 practicing physicians; Nil residents, interns Armed Forces
‡834—Practical Diagnosis and Management of Cardiovascular Diseases	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Hotel Statler and Los Angeles County Hospital	G Lim 100	IC	Lec, Pan, O	21	9/18/59	9/20/59	C; 3 days	65
‡833—Bedside Cardiology	University of *Southern* California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G Lim 65	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O	21	2/ 4/60	4/21/60	I; 12 sessions 2 hr weekly Wednesdays	65
‡843—Symposium on *Hypertension*	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Hotel Statler, Los Angeles	G Lim 100	O	Lec, Pan, O, AV	7	3/11/60	3/11/60	C; 1 day	25
9th Annual Symposium on Heart Disease—"A Program for Clinicians",	San Diego County Heart Association 3545 Fourth Ave., San Diego, Calif.; course at El Cortez Hotel, San Diego	B	IC	PD, Lec, Pan, O, AV	10½	10/ 5/59	10/ 6/59	C; 1½ days	5
Twenty-Ninth Annual Postgraduate Symposium on Heart Disease	San Francisco Heart Association, Inc. 229 Geary St., San Francisco 2; course at St. Francis Hotel, San Francisco	B	IO	PD, Clin C, Sem, Lec, Pan, O, AV	21	9/30/59	10/ 2/59	C; 3 days	Unknown
Symposium on Heart Disease	*Orange County Heart Association* P. O. Box 1704, Santa Ana, Calif.	G	IC	Surg, Lec, Pan, O, AV	8-10	Spring/60		C; 1 day	12.50
Symposium on Cardiovascular Diseases	Santa Barbara County Heart Association 18 *La Arcada* Court, Santa Barbara, Calif.; course at Biltmore Hotel, Santa Barbara	B Lim 100	IC	Sem, Lec, Pan, O, AV	8	Unknown		C; 1 day	20
Annual Heart Symposium	Sonoma County Heart Association Rosenberg Building, Santa Rosa, Calif.	G	IC	**Lec**, Pan, O, AV	6-8	Fall/59		C; 1 day	15
Western Cardiac Conference	Colorado Heart Association 1636 Logan St., Denver	G	IC	Lec, Pan, O, AV	30	8/15/60	8/19/60	C; 5 days	10 to 30
9th Annual Western Cardiac Conference	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	PD, Sem, Lec, Pan, O, AV	40	8/22/60	8/26/60	C; 5 days	Unknown
Heart Symposium (9th Annual)	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	2/10/60	2/10/60	C; 1 day	Nil
Diagnosis and Treatment of Heart Disease, Including Special Tests	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	11	4/20/60	4/21/60	C; 2 days	20
Midwest Cardiac Conference	Iowa Heart Association 2100 Grand Ave., Des Moines; course at State University of Iowa Iowa City	G	IC	Clin C, Lec, Pan, O, AV	10	11/13/59	11/15/59	C; 3 days	Nil
Cardiology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 10	PT	Lab, BR, Clin C, Sem, Lec, O, AV, EPP		9/15/59	6/15/60	9 mo.	600
The Heart: Rheumatic and Congenital Heart Disease	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	28	1/18/60	1/21/60	C; 4 days	75
Clinical Traineeship in Cardiovascular Disease	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Lab, BR, Clin C, Lec, O, AV, EPP	120	2/ 1/60 3/ 1/60	2/29/60	30 days	200
Cardiovascular Disease	Harvard Medical School 25 Shattuck St., Boston; course at *Massachusetts General Hospital*, Boston 14	S Lim 12	IC	Lab, PD, LC, BR, Clin C, Lec, O	35-40 per week	10/ 1/59	5/31/60	C, unknown	800

Key will be found on page 1938.

CARDIOVASCULAR DISEASE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Cardiology 1	Harvard Medical School 25 Shattuck St., Boston; course at Beth Israel Hospital, Boston 15	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Lec, O	450	2/ 1/60	4/30/60	C; 65 days	500
Diseases of the Heart	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Lim 10	IC	PD, Clin C, Lec, O, AV	34	3/21/60	3/25/60	C; 5 days	50
Cardiovascular Diseases for General Physicians and Specialists	Continuation Medical Education 1312 Mayo Memorial University of Minnesota, Minneapolis 14	B	IC	Lec, Pan, O, AV	15	2/ 8/60	2/10/60	C; 3 days	40
Cardiovascular Seminar	University of Mississippi Medical Center 2500 N. State St., Jackson, Miss.	B Lim 200	IC	PD, Sem, Lec, Pan, O, AV	20	4/ 6/60	4/ 8/60	C; 3 days	10
Cardiac Arrest and Resuscitation	University of Missouri School of Medicine 807 Stadium Rd., Columbia, Mo.	G Lim 20	IC	Lab, PD, Clin C, Lec, Pan, O, AV, EPP	6-8	Arranged		C; 1 day	35
Cardiac Auscultation	Dr. Donald W. Bussmann St. Louis University School of Medicine 1325 So. Grand Blvd., St. Louis 4; course at Cardinal Glennon Memorial Hospital, St. Louis	G Lim 35	IC	Lec, Pan, O, AV	13½	12/ 2/59	12/ 3/59	C; 2 days	50
Recent Advances in Clinical Cardiology	St. Michael's Hospital 306 High St., Newark, N. J.	G Lim 60	II	PD, LC, BR, Clin C, Lec, O, AV	24	9/59	3/60	I; Unknown	30
Acute Cardio-Respiratory Failure with Resuscitation	St. Michael's Hospital 306 High St., Newark, N. J.	B Lim 12	IC	Lec, O, AV, EPP	6	10/59 Repeated monthly on Saturdays	same day	C; 1 day	25
Clinical Cardiology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Paterson General Hospital, Paterson, N. J.	G Lim 10	II	PD, Clin C, Lec, O, AV	15	10/ 1/59	12/10/59	I; 10 sessions 1½ hr. weekly, Thursdays	50
Selected Topics in Advanced Cardiology	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Fitkin Memorial Hospital, Neptune, N. J.	G Lim 10	II	PD, Clin C, Lec, Pan, O, AV	15	2/ 2/60	4/ 5/60	I; 10 sessions 1½ hr. weekly, Tuesdays	50
Special Teaching Day in Cardiovascular Diseases	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	Sem, Lec, Pan, O, AV	5	2/11/60	2/11/60	C; 1 day	12
Cardiovascular Disease	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O	14	11/11/59	11/12/59	C; 2 days	30
Medicine PM 64—Surgical Treatment of Heart Diseases (Sect. A & B)	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, LC, Clin C, Sem, Lec, O, AV	63	9/22/59 2/ 2/60	1/26/60	I; 18 sessions 3½ hr. weekly, Tuesdays	Unknown
Medicine PM 60—Cardiology, I, Sect. A & B	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, Lec, O, AV	96	9/24/59 2/ 4/60	1/28/60	I; 16 sessions 6 hr. weekly, Thursdays	150
Medicine PM 62—Cardiology II, Sections A & B	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, LC, Lec, O, AV	56	9/24/59 2/ 4/60	1/28/60	I; 16 sessions 3½ hr. weekly, Thursdays	150
Medicine PM 63—Cardiology III, Section A & B	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 20	II	PD, Clin C, Sem, Lec, O, AV	56	9/24/59 2/ 4/60	1/28/60	I; 16 sessions 3½ hr. weekly, Thursdays	150
Medicine PM 29—Clinical Cardiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	PD, LC, Lec, O	20	10/13/59 2/ 2/60	12/15/59	I; 10 sessions 2 hr. weekly, Tuesdays	60
Medicine PM 31—Recent Advances in Cardiovascular Disease	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	IC	Lab, PD, Clin C, Lec, O, AV	30	1/25/60	2/ 5/60	C; 10 days	75
Medicine PM 18—Heart Disease and Circulatory Dynamics	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	PD, LC, BR, Lec, O, AV, EPP	20	2/16/60	4/19/60	I; 10 sessions 2 hr. weekly, Tuesdays	50

Clinical Cardiology	New York Medical College *Flower and Fifth Ave. Hospitals* Fifth Ave., and 106th St., New York; course at Metropolitan Hospital, New York	G Lim 25	II	PD, BR, Lec	20	9/ 9/59	2/ 3/60	I; 20 sessions 1 hr. weekly, Wednesdays	100
2548—Diagnostic Cardiac Auscultation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 10	IC	Lab, PD, Lec, O, AV	24	10/28/59 2/24/60	10/31/59	C; 3½ days	60
Postgraduate Course in Cardiology	St. Francis Hospital and Sanatorium Roslyn, N. Y.	G Lim 60	IC	PD, Sem, Surg, Lec, Pan, O, AV, TV	14	4/18/60	4/23/60	C; 6 days	Unknown
Seminars on Heart Disease	St. Francis Hospital and Sanatorium Roslyn, N. Y.	G Lim 75	II	Sem, Lec, O	8	9/59	5/60	I; 4 sessions	Nil
Recent Advances in Cardiovascular Disease	Huron Road Hospital 13951 Terrace Rd., Cleveland	G Lim 125	IC	Sem, Lec	14	10/10/59	10/17/59	C; 2 days	25
Cardiac Arrest and Resuscitation	Mercy Hospital Research Foundation 2221 Madison Ave., Toledo, Ohio	B Lim 15	O	Lab, Lec, O, AV, EPP	4	4th Wednesday each mo.	same day	C; 1 session, 4 hr.	Nil
Clinical Cardiology	American College of Physicians 4200 Pine St., Philadelphia 4; *course at* Tulane University School of Medicine, New Orleans	S Lim 60	IC	PD, Lec, Pan, O	35-50	11/30/59	12/ 4/59	C; 5 days	60 members; 80 non-members
Postgraduate Cardiology Course #1—General Cardiology Including Electrocardiography	Hahnemann Medical College and Hospital 230 N. Broad St., Philadelphia 2	G Lim 50	II	PD, Lec, Pan, O, AV	90	10/59	5/60	I; 30 sessions 3 hr. weekly, Thursdays	150
Postgraduate Cardiology Course #2—Electrocardiography, Cardiac Auscultation, Cardiac Roentgenology	Hahnemann Medical College and Hospital 230 N. Broad St., Philadelphia 2	G Lim 20	II	PD, Lec, Pan, O, AV	56	10/59	6/60	I; 30 sessions 1½ hr weekly, Thursday	150
Clinical Cardiology	Pennsylvania Hospital 8th and Spruce Sts., Philadelphia 7	G Lim 24	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	55	1/ 7/60	3/10/60	I; 10 sessions 5½ hr weekly, Thursdays	Unknown
Practical Cardiology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at *University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.*	B Lim 200	IC	Lec, Pan, O, AV	20	11/30/59	12/ 4/59	C; 5 days	30
Arrhythmias—Recent Advances in Physiology Cardiac Pacemakers; Fundamental Aspects of Drugs Commonly Used	University of Washington School of Medicine Seattle, Wash.	G	IC	PD, Clin C, Sem, Lec, O, AV		11/59			Unknown

CHEST DISEASE
(See also Endoscopy)

12th Annual Symposium on Pulmonary Diseases	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20 course at Fitzsimons Army Hospital, Denver 8	B	IC	PD, Sem, Lec, Pan, O, AV	50	9/14/59	9/18/59	C; 5 days	5
Cardiopulmonary Disease Seminars	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	PD, Sem, Lec, Pan, O, AV	12	10/30/59	10/31/59	C; 1½ days	Unknown
Conference on Research in Emphysema: Air Pollution	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	Sem, Lec, Pan, O, AV	24	6/60	6/60	C; 3 days	Unknown
Symposium on Pulmonary Disease	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D. C. course at Fitzsimons Army Hospital, Denver	G Lim 75	IC	LC, Lec, Pan, AV	40	9/14/59	9/18/59	C; 5 days	5 (non-military)
Fourteenth Annual Postgraduate Course—Clinical Cardiopulmonary Physiology	American College of Chest Physicians 112 E. Chestnut St., Chicago; course at Edgewater Beach Hotel, Chicago	B Lim 100	IC	Lec, Pan, O, AV	35	10/ 5/59	10/ 9/59	C; 5 days	75 members; 100 non-members
Twelfth Annual Postgraduate Course on Diseases of the Chest	American College of Chest Physicians 112 E. Chestnut St., Chicago 11; course at Park Sheraton Hotel, New York	B Lim 100	IC	Lec, Pan, O, AV	35	11/ 9/59	11/13/59	C; 5 days	75 members; 100 non-members
Fifth Annual Postgraduate Course on Diseases of the Chest	American College of Chest Physicians 112 E. Chestnut St., Chicago 11; course at Ambassador Hotel, Los Angeles	B Lim 100	IC	Lec, Pan, O, AV	35	12/ 7/59	12/11/59	C; 5 days	75 members; 100 non-members
Thirteenth Annual Postgraduate Course on Diseases of the Chest	American College of Chest Physicians 112 E. Chestnut St., Chicago 11; course at Sheraton Hotel, Philadelphia	B Lim 100	IC	Lec, Pan, O, AV	35	3/14/60	3/18/60	C; 5 days	75 members; 100 non-members
Clinical Traineeship in Pulmonary Disease	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Lab, BR, Clin C, Lec, O, AV, EPP	160	11/ 2/59 1/ 4/60 4/ 1/60 5/ 2/60	11/30/59	30 days	50 mo. Kansas residents; 100 mo. non-residents
Medical-Surgical Symposia—Part I. Pulmonary Disease	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	O	PD, LC, Sem, Lec, Pan, O, AV, TV	7	3/21/60	3/21/60	C; 1 day	20

Key will be found on page 1938.

CHEST DISEASES—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Pulmonary Diseases	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	Lab, PD, Clin C, Lec, O, AV	18	3/14/60	3/16/60	C; 3 days	40
One Day Seminar on Diseases of the Chest	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark 2, N. J.; course at Elizabeth General Hospital, Elizabeth, N. J.	G Lim 40	IC	Sem, Lec, Pan, O, AV	8	10/14/59	10/14/59	C; 1 day	25
Clinical Cardiopulmonary Physiology; Children and Adults	Dr. Burgess L. Gordon, Director of Education, Lovelace Foundation 4800 Gibson Blvd., S. E., Albuquerque, N. Mex.	G	II	Clin C, Sem, Lec, EPP	10	Fall/59	Spring/60	I; 3 days	Nil
Medicine PM 80	Dean of Faculty of Medicine, Columbia University College of Physicians and Surgeons 630 W. 168th Street, New York 32; course at Bellevue Hospital, New York	S Lim 60	IC	BR, Clin C, Lec, O, AV	161	10/ 1/59 2/ 1/60	10/31/59	C; 23 days	175 first mo.; 75 for additional periods
Medicine PM 71	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32 course at Montefiore Hospital, New York 67	S	II	PD, Sem, Lec, O, AV	52½	1/ 5/60	5/31/60	I; 21 sessions 2½ hr. weekly Tuesdays	100
Eighth Annual Symposium for General Practitioners on Tuberculosis and Other Chronic Pulmonary Disease	Saranac Laboratory 7 Church St., Saranac Lake, New York, and Ray Brook State Tuberculosis Hospital, Ray Brook, New York	G Lim 75	IC	PD, LC, BR, Lec, Pan, O	26	Summer/60		C; 5 days	50
Fourth Biennial Postgraduate Course on Pulmonary Diseases	Ohio State University College of Medicine 11th and Neil Aves., Columbus 10, Ohio	G	IC	Lec, Pan, O, AV	15	9/25/59	9/26/59	C; 2 days	25
Bronchoesophagology—Diagnosis and Treatment of Diseases of Bronchi, Lungs and Esophagus	Chevalier Jackson Clinic, Temple University Medical Center 3401 N. Broad St., Philadelphia 40	B Lim 20	IC	Lab, PD, LC, Clin C, Sem, Lec, Pan, O, AV	80	11/ 9/59	11/20/59	C; 11 days	250

CLINICAL PATHOLOGY
(See also Basic Sciences)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Laboratory Methods in the Diagnosis of Viral and Rickettsial Diseases	Communicable Disease Center Laboratory Branch Training Office, Box 185, Chamblee, Ga.; course at Communicable Disease Center, Virus Laboratory, Montgomery, Ala.	G and others Lim 15	IC	Lab, Sem, Lec, O, AV, EPP	120	9/27/59	10/16/59	C; 15 days	Nil
#849—Laboratory Methods	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33 course at Hotel Statler, Los Angeles	G Lim 75	IC	Lec, Pan, O, AV	7	10/ 9/59	10/ 9/59	C; 1 day	25
Laboratory Medicine	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 9	II	Lab, Lec, O, AV	48	Arranged		I; 24 sessions 2 hr. weekly, Fridays	150
The Precipitin Reaction	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G Lim 15	II	Lec	6	Arranged		Arranged	60
Laboratory Aids in Diagnosis and Treatment	Dr. Glenn W. Pfister, Jr., Secretary Southwestern Ohio Society of General Physicians—Educational Committee 1710 Section Rd., Cincinnati 37; course at University of Cincinnati College of Medicine, Cincinnati	G	IC	Sem, Lec, Pan, AV	4½	5/ 1/60	5/ 1/60	C; 1 day	10
Protozoology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston, 25, Tex. course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.	G and residents Lim 6	II	Lab, Lec, EPP	40	12/ 1/59	2/11/60	I; 20 sessions 2 hr. weekly, Tuesdays, Thursdays	40

DERMATOLOGY
(See also Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship and Special Skills Course—Dermatology	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
#880—Dermatology and Syphilology	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G Lim 15	IC or PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan	1 yr.	9/15/59	8/15/60	C; 1 yr.	1,000
#843—Dermatology Clinic	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33 course at Los Angeles County Hospital	G Lim 35	IC	LC, BR	7	3/24/60	3/24/60	C; 1 day	25

Dermatology Clinics	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	PD, LC, Lec, Pan, O, AV	14	Spring/60		C; 2 days	Unknown
Dermatology for General Practitioners	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	G	IC	PD, Sem, Lec, Pan, O, AV	24	7/11/60	7/16/60	C; 3 days	35
Clinical Dermatology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 9	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O	120	Arranged	4 wk. later	24 days	125
Course II in Dermatology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 15	IC	Lab, PD, LC, BR, Clin C, Lec, O	60	11/ 9/59 Spring/60	11/20/59	C; 11 days	150
Dermatology and Syphilology 1	Harvard Medical School 25 Shattuck St., Boston course at Massachusetts General Hospital, Boston	S Lim 6	IC	Lab, PD, LC, BR, Clin C, Sem, Lec	35-40 hr. wk.	10/ 1/59	9/30/60	C; 11 mo.	800
Dermatology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	15	10/22/59	10/24/59	C; 3 days	40
Dermatology	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV	14	11/18/59	11/19/59	C; 2 days	30
Dermatology PM 60—Common Skin Diseases — Treatment	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32 course at Montefiore Hospital, New York 67	G	II	Lab, PD, Lec, O, AV, EPP	20	1/ 4/60	3/14/60	I; 10 sessions 2 hr. weekly, Mondays	40
#521—Dermatology and Syphilology (Designed for Pediatricians)	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, AV	35	10/ 5/59	10/ 9/59	C; 5 days	100
#522—Comprehensive Review in Dermatologic Histopathology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 15	IC	Lab, Sem, Surg, Lec, Pan, O, AV	35	1/ 4/60	1/ 8/60	C; 5 days	100
#523—Seminar in Dermatology and Syphilology (Designed for General Physicians)	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, LC, Clin C, Sem, Surg, Lec, Pan, O, AV	35	2/15/60	2/19/60	C; 5 days	100
#524—Symposium on Dermatology and Syphilology (For Dermatologists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 30	IC	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, AV	35	5/16/60	5/20/60	C; 5 days	125
Dermatology	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 7	II	PD, LC, Surg, O, EPP	20	10/ 8/59	12/17/59	I; 10 sessions 2 hr. weekly, Thursdays	35
Dermatology Advances	American College of Physicians 4200 Pine St., Philadelphia 4 course at University of Michigan Medical School, Ann Arbor, Mich.	S	IC	PD, Lec, O	35-40	3/21/60	3/25/60	C; 5 days	60 A.C.P. members; 80 non-members
Dermatology and Syphilology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex. course at Turner Home, El Paso, Tex.	G Lim 60	IC	Lec, AV	7	12/ 6/59	12/ 6/59	C; 1 day	10

ELECTROCARDIOGRAPHY

Advanced Clinical Electrocardiography	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 25	II	Sem, Lec, Pan, O, AV	20	10/6/59	12/8/59	I; 10 sessions 2 hr. weekly, Tuesdays	60
#835—Basic Home Course in Electrocardiography	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G	HS(C)	HS(C)	52-100	Any time	52 weeks later	Weekly mailing	100
#836—Advanced Home Course in Electrocardiography	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G	HS(C)	HS(C)	52-100	Any time	52 weeks later	Weekly mailing	85
Vectorcardiography	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 75	IC	Lec, O, AV	7	9/59	9/59	C; 1 day	20
Fundamentals of Electrocardiography	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	G	II	Lec	12-15	10/59	12/59	I; 9-10 sessions 1½ hr. weekly, Mondays	10
Medicine 210—Clinical Electrocardiography	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	G Lim 30	II	Lec, O, AV, EPP	12	9/22/59	12/8/59	I; 12 sessions 1 hr. weekly, Tuesdays	50

Key will be found on page 1938.

ELECTROCARDIOGRAPHY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
1) Basic Electrocardiography 2) Electrocardiography of Myocardial Infarction	Mount Sinai Hospital of Greater Miami 1300 Alton Rd., Miami Beach, Fla.	G Lim 30	H	Lec, AV	1) 24 2) 12	10/ 5/59	12/28/59	I; 1) 24 sessions 2) 12 sessions 1 hr. thrice weekly, Mondays, Wednesdays, Fridays	25
Advanced Electrocardiography	Emory University School of Medicine 69 Butler St., S.E., Atlanta 3, Ga.	S	IC	Unknown	24	3/ 3/60	3/ 5/60	C; 3 days	Unknown
Interpretation of Complex Arrhythmias	Michael Reese Hospital, Cardiovascular Department, 29th St. and Ellis Ave., Chicago	G	IC	Sem, O, AV, EPP	30	12/ 7/59	12/11/59	C; 5 days	100
Electrocardiography and Heart Disease	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 30	IC	Lab, PD, LC, BR, Sem, Lec, O, AV, EPP	70	10/5/59 Spring/60	10/16/59	C; 11 days	150
One Week Advanced Course in Electrocardiography	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 30	IC	Lab, Lec, Pan, AV, EPP	40	6/60	5 days later	C; 5 days	100
Electrocardiographic Interpretation	Michael Reese Hospital, Cardiovascular Department, 29th St. and Ellis Ave., Chicago	G	IC	Sem, Lec, O, EPP	80	8/17/60	8/29/60	C; 12 days	150
Basic Electrocardiography	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	21	9/23/59	9/25/59	C; 3 days	30
Interpretation of Electrocardiograms—I	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	AV	13	10/ 2/59 3/25/60	3/25/60	26 weekly lessons	25
Interpretation of Electrocardiograms—II	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	AV	13	10/15/59 4/21/60	4/ 7/60		17
Interpretation of Electrocardiograms—III	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	AV	18	11/18/59	7/20/60	36 weekly lessons	40
Clinical Electrocardiography	Maine Medical Center 22 Bramhall St., Portland, Me.	G Lim 100	H	Clin C, Lec, O, AV	10	1/ 6/60	3/ 9/60	I; 10 sessions 1 hr. weekly, Wednesdays	Nil
Practical Electrocardiography 2—Elementary Electrocardiographic Interpretation	Harvard Medical School 25 Shattuck St., Boston; course at Beth Israel Hospital, Boston	G Lim 36	H	Lab, Lec, O, AV, EPP	30	10/ 7/59	12/ 9/59	I; 10 sessions 3 hr. weekly, Wednesdays	100
Practical Electrocardiography 1—Elementary Electrocardiographic Interpretation	Harvard Medical School 25 Shattuck St., Boston; course at Beth Israel Hospital, Boston	G Lim 36	IC	Lab, Lec, O, AV, EPP	30	11/ 2/59	11/ 6/59	C; 5 days	100
Electrocardiographic Clinics 2—Applied Electrocardiography and Cardiology	Harvard Medical School 25 Shattuck St., Boston; course at Beth Israel Hospital, Boston	G Lim 10	H	Lab, Sem, Lec, O, AV, EPP	30	3/ 2/60	5/11/60	I; 10 sessions 3 hr. weekly, Wednesdays	150
Electrocardiographic Clinics 1—Applied Electrocardiography and Cardiology	Harvard Medical School 25 Shattuck St., Boston; course at Beth Israel Hospital, Boston	G Lim 10	IC	Lab, Sem, Lec, O, AV, EPP	30	4/25/60	4/29/60	C; 5 days	150
Clinical Electrocardiography	Harvard Medical School 25 Shattuck St., Boston; course at Peter Bent Brigham Hospital, Boston 15	S Lim 50	IC	Lab, Clin C, Lec, O	35	6/13/60	6/17/60	C; 5 days	125
Electrocardiography I	Tufts University School of Medicine 136 Harrison Ave., Boston; course at New England Center Hospital 171 Harrison Ave., Boston	G Lim 25	IC	Lec, O, AV	25	12/ 7/59	12/11/59	C; 5 days	60
Electrocardiography II—Advanced	Tufts University School of Medicine 136 Harrison Ave., Boston; course at New England Center Hospital 171 Harrison Ave., Boston	G Lim 30	IC	Lec, O, AV	20	4/11/60	4/13/60	C; 3 days	30
Basic Electrocardiography	Highland Park General Hospital 389 Glendale, Highland Park, Mich.	S and medical residents Lim 30	H	Clin C, Sem, Lec, O, AV	25	10/59	3/60	I; 25 sessions 1¼ hr. weekly, Fridays	Unknown
Electrocardiographic Diagnosis	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	Lab, Lec, O, AV	35	3/28/60	4/ 2/60	C; 5½ days	75
Intermediate Electrocardiography for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV, EPP	30	5/ 2/60	5/ 6/60	C; 5 days	65
Advanced Electrocardiology	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	Clin C, Sem, Lec, O, AV	18	9/28/59	9/30/59	C; 3 days	30
Advanced Clinical Electrocardiography	St. Michael's Hospital 306 High St., Newark, N.J.	B Lim 65	H	Lec, O, AV	20	9/59	2/60	I; 20 sessions 1 hr. weekly, Wednesdays	30

grams with Disease Processes (Hospitalized Patients)	47 New Scotland Ave., Albany 8, N.Y.							2 hr. weekly	
E.C.G. Interpretation	*Joint Committee* on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N.Y.; *course at Beth-El Hospital, Brooklyn, N.Y.*	G Lim 20	II	Lec, O	12	10/59	11/59	I; 12 sessions 1 hr. twice weekly Mondays, Fridays	20
Medicine PM 63A—Clinical Electrocardiography: *Sections A & B*	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, BR, Lec, O, AV	36	9/22/59 2/2/60	1/26/60	I; 18 sessions 2 hr. weekly, Tuesdays	100
Medicine PM 40—Electrocardiography	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; *course at Mount Sinai Hospital, New York 29*	G Lim 30	IC	Lec, O	30	10/12/59 1/11/60	10/23/59	C; 10 days	75
Medicine PM 43—Spatial Vectorcardiography and Vector Interpretation	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; *course at Mount Sinai Hospital, New York 29*	G	IC	PD, Lec, O, AV	25	11/30/59	12/4/59	C; 5 days	75
Interpretation of Electrocardiograms	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G Lim 15	II	Lec, AV	20	9/9/59	2/3/60	I; 20 sessions 1 hr. weekly, Wednesdays	100
#546—Fundamentals of Clinical Electrocardiographic Interpretation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	II	*Lab*, *Lec*, *O*	36	11/1/59	3/16/60	I; 18 sessions 2 hr. weekly, Wednesdays	75
#545—Electrocardiography	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	IC	PD, Lec, O, AV	35	11/9/59 3/14/60	11/14/59	C; 6 days	100
#547—The Physiological Basis of Clinical Electrocardiography *(An advanced course in Electrocardiography)*	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	IC	Lab, Lec, O	38	6/6/60	6/11/60	C; 5½ days	85
Basic Electrocardiography	Albert Einstein Medical Center Southern Division Fifth and Reed Sts., Philadelphia 47	G Lim 30	II	PD, Lec, AV	45	10/21/59	2/17/60	I; 15 sessions 3 hr. weekly, Wednesdays	75
Advanced Electrocardiography	Albert Einstein Medical Center Southern Division Fifth and Reed Sts., Philadelphia 47	G Lim 12	II	Lab, PD, Lec, EPP	30	2/24/60	4/27/60	I; 10 sessions 3 hr. weekly, Wednesdays	50
Seminar on the Electrocardiographic *Exercise Test*	E. Lepeschkin, M.D., Division of Experimental Medicine University of Vermont, College of Medicine Burlington, Vt.; *course at DeGoesbriand Memorial Hospital* 1 S. Prospect St., Burlington, Vt.	S Lim 100	IC	Sem, Lec, Pan, O	18	9/19/59	9/20/59	C; 2 days	10 for non-residents of Vt.
Electrocardiography—Clinical Interpretation	*University of Washington School of Medicine* Seattle, Wash.	G	IC	Lab, Sem, Lec, O, AV, EPP		11/59			Unknown

ENDOCRINOLOGY

Endocrinology Clinics	California Medical Association 2975 Wilshire Blvd., Los Angeles; *course at University of Southern California School of Medicine, Los Angeles*	G Lim 75	IC	PD, LC, BR, Pan, O	9	2/21/60	2/23/60	C; 3 days	25
The Dynamics of Endocrine and Metabolic Disease	The Highland-Alameda County Hospital, Institute for Metabolic Research 2701 14th Ave., Oakland, Calif.	S Lim 100	IC	Lec, Pan, O	24	2/ 8/60	2/10/60	C; 3 days	60
Eleventh Postgraduate Assembly in Endocrinology and Metabolism	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 100	IC	PD, Lec, Pan, O, AV	42	11/ 9/59	11/13/59	C; 6 days	100
Clinical Endocrinology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 5	IC	Lab, PD, LC, BR, Clin C, Lec, O, EPP	35	10/ 5/59 Spring/60	10/19/59	C; 5 days	100
Diagnosis and Treatment *of Common* Endocrine Disorders	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	14	5/18/60	5/19/60	C; 2 days	20
Medical-Surgical Symposia—Part V. Endocrinology and Metabolism	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	O	PD, LC, Sem, Lec, Pan, O, AV	7	3/25/60	3/25/60	C; 1 day	20
Endocrinology with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	B Lim 10	IC or PT	PD, Clin C, Lec, O, AV	60	2/ 1/60	2/13/60	*C; 10 days*	50
Endocrinology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	30	3/28/60	4/ 1/60	C; 5 days	65

Key will be found on page 1938.

ENDOCRINOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Endocrine Disease	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV	14	10/28/59	10/29/59	C; 2 days	30
Metabolic Endocrinology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y. course at Maimonides Hospital, Brooklyn, N. Y.	G Lim 20	II	PD, Lec, O	15	10/59	12/59	I; 10 sessions 1½ hr. weekly, Tuesdays	20
Clinical Endocrinology	Albert Einstein Medical Center Southern Division Fifth and Reed Sts., Philadelphia 47	G Lim 25	II	PD, LC, Lec, Pan, AV	39	12/ 2/59	3/ 2/60	I; 13 sessions 3 hr. weekly Wednesdays	60

ENDOSCOPY

(See also Gastroenterology, Gynecology, Obstetrics and Gynecology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Bronchoscopy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 2	IC	Lab, PD, LC, Surg, Lec, O, EPP	15	9/14/59 10/12/59 11/16/59 Offered in 1960 each mo. except July and August	9/19/59	C; 5 days	100
Ten-Day Practical Course in Cystoscopy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 2	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, EPP	30	9/14/59 10/12/59 11/ 9/59 11/30/59 Every 2 wk. during 1960	9/25/59	C; 10 days	150
Endoscopy	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex; course at University of Texas M.D. Anderson Hospital and Tumor Institute Houston, Texas	G Lim 1	II	Lab, PD, LC, BR, Sem, Lec, EPP	65	1/ 7/60	6/23/60	I; 25 sessions 2½ hr. weekly Thursdays	100

EPHEBOLOGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Adolescents	University of California Medical Center Second and Parnassus Ave., San Francisco; course at Children's Hospital, San Francisco	G Lim 100	IC	Lec, Pan, O, AV	7	11/14/59	11/14/59	C; 1 day	12.50
Adolescent Medicine 1	Harvard Medical School 25 Shattuck St., Boston; course at Children's Hospital, Boston	G Lim 2	IC	PD, LC, BR, Clin C, Sem, Lec	35-40	Arranged		C; Unknown	300 first three mos. Nil there after

FRACTURES

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Fractures in General Practice	Medical College of Georgia Augusta, Ga.	G Lim 20	IC	PD, LC, Clin C, Sem, Lec, Pan	16	12/ 1/59	12/ 3/59	C; 3 days	25
Care and Treatment of Fractures	American Fracture Association Bloomington, Ill; course at Tulane University and Roosevelt Hotel, New Orleans	B	IC	PD, Sem, Lec, Pan, O	Unknown	Unknown			Unknown
Course II in Clinical Fractures	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	PD, LC, BR, Clin C, Surg, Lec, O	35	Arranged	Saturday following starting date	5 days	50
Course III in Fractures and Traumatic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Surg, Lec	86	10/12/59 4/60 6/60	10/21/59	C; 11 days	150
Fractures	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Lec, Pan, O, AV	14	11/23/59	11/24/59	C; 2 days	30
Fractures for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	18	11/16/59	11/18/59	C; 3 days	40
Fifth Annual Postgraduate Course in Fractures and Other Trauma	Dr. Preston A. Wade Cornell University Medical College 1300 York Ave., New York 21	S	IC	Clin C, Sem, Lec, Pan, O	44	6/13/60	6/18/60	C; 6 days	150
Fractures and Allied Trauma	New York Medical College Flower and Fifth Ave., Hospitals Fifth Ave., and 106th St., New York	G Lim 6	IC	PD, LC, BR, Clin C, Surg, Lec, AV	90	10/ 5/59 3/ 7/60	10/23/59	C; 15 days	200
Fractures	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.;	G	IC	Lec, AV	8	1/21/60	1/21/60	C; 1 day	10

	1400 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.								

GASTROENTEROLOGY

Diarrhea	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	9	11/ 6/59	11/ 7/59	C; 2 days	35
2846-Advances in the Diagnosis and Treatment in Gastroenterology	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33 course at Hotel Statler, Los Angeles	G Lim 100	IC	Lec, Pan, O	21	1/15/60	1/17/60	C; 3 days	65
Gastroscopy and Gastroenterology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 5	IC	Lab, PD, LC, BR, Lec, O, EPP	10	9/14/59 11/ 2/59 3 dates in 1960	9/26/59	C; 12 days	200
Clinical Traineeship in Gastroenterology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Lab, BR, Clin C, Lec, O, AV, EPP	Arranged	Arranged			50 mo. residents of Kansas; 100 mo. nonresidents
Medical-Surgical Symposia—Part II. Gastroenterology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	O	PD, LC, Sem, Lec, Pan, O, AV, TV	7	3/22/60	3/22/60	C; 1 day	20
Gastroenterology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	Lab, PD, Clin C, Lec, O, AV	20	2/22/60	2/24/60	C; 3 days	40
Postgraduate Gastroenterology	American College of Gastroenterology 33 W. 60th St., New York 23; course at Biltmore Hotel, Los Angeles	G	IC	Clin C, Lec, Pan	15	9/24/59	9/26/59	C; 3 days	35 for members; 50 for nonmembers
Medicine PM 70	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 20	II	PD, BR, Lec, O, AV	52½	9/ 8/59	12/22/59	I; 15 sessions 3½ hr. weekly, Tuesdays	75
Medicine PM 73—Advanced Gastroenterology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 10	II	PD, BR, Sem, Lec, O, AV	56	1/12/60	5/ 3/60	I; 16 sessions 3½ hr. weekly, Tuesdays	75
Medicine PM 45—Gastroenterology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	IC	PD, LC, BR, Lec, O, AV	30	4/ 4/60	4/ 8/60	C; 5 days	75
Advanced Gastroscopy—Instrumentation and Interpretation	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave., and 106th St., New York; course at Metropolitan Hospital, New York	S Lim 5	II	PD, LC, Clin C, Lec	20	Arranged		I; 10 sessions 2 hr. ea.	250
Gastroenterology	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec, O, EPP	15	4/ 1/60 10/ 1/60	4/ 6/60	C; 5 days	50
Gastroenterology	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 20	II	Lab, PD, LC, BR, Sem, Lec, Pan, O, AV, EPP	20	11/ 4/59	1/27/60	I; 10 sessions 2 hr. weekly, Wednesdays	50
Current Concepts	American College of Physicians 4200 Pine St., Philadelphia 4; course at Louisiana State University School of Medicine 1542 Tulane Ave., New Orleans	S	IC	PD, Lec, O	15-35	3/21/60	3/23/60	C; 3 days	60 A.C.P. members; 80 nonmembers
Gastroenterology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.	G Lim 200	IC	Lec, Pan, AV	16	2/25/60	2/27/60	C; 2½ days	Unknown

GENERAL MEDICINE

(See also all other categories)

John A Andrew Clinical Society	Secretary, John A Andrew Memorial Hospital of Tuskegee Institute Tuskegee Institute, Ala.	G Lim 500	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	30	4/24/59	4/29/59	C; 6 days	15
Emotional Problems in Office Practice	University of California Los Angeles Residential Conference Center, Lake Arrowhead, Calif.; course at University of California Medical Center Los Angeles 24	G Lim 25	II	Sem, Lec, Pan, O, AV	120	9/19/59	6/19/60	I; Unknown	200

Key will be found on page 1938.

GENERAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Postgraduate Medical Lecture Series	St. Mary's Long Beach Hospital 509 E. 10th St., Long Beach, Calif.	G	II	Clin C, Lec, Pan, O, AV	24	3/60		I; 12 sessions 2 hr. weekly, Tuesdays	50
Alumni Postgraduate Convention	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV, TV	12	2/28/60	2/29/60	C; 2 days	10 each course or all 4 for 30
Regional Postgraduate Institute for North Coast County Societies	California Medical Association, 2975 Wilshire Blvd., Los Angeles; course at Hoberg's Resort, Lake County	G	IC	Sem, Lec, Pan, O, AV	12	Unknown	Unknown	C; 2 days	25
Regional Postgraduate Institute for Southern County Societies	California Medical Association, 2975 Wilshire Blvd., Los Angeles; course at Oasis Hotel and Local Theater, Palm Springs	G	IC	Sem, Lec, Pan, O, AV	12	4/14/60	4/15/60	C; 2 days	25
Regional Postgraduate Institute for Sacramento Valley County Societies	California Medical Association, 2975 Wilshire Blvd., Los Angeles; course at Tahoe Tavern, Tahoe City	B	IC	Sem, Lec, Pan, O, AV	10	6/23/60	6/24/60	C; 2 days	25
Teaching Clinics in Medicine, Surgery, Obstetrics, Etc.	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 75	II	Sem, Lec, Pan, O, AV	24	9/17/59	12/10/59	I; 12 sessions 2 hr. weekly, Thursdays	50
Common Problems of the Foot	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	9	9/18/59	9/19/59	C; 2 days	35
Arthritis and Rheumatism	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	12	12/59		C; 2 days	50
Management of Medical Emergencies	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	12	Spring/60		C; 2 days	50
#819—The Doctor and the Family (Problem Children, Sexual Problems, Etc.)	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Hotel Statler, Los Angeles	G Lim 100	IC	Lec, Pan, O	7	10/16/59	10/16/59	C; 1 day	25
Recent Advances in Medicine (Homecoming) #842	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Los Angeles County Hospital and Hotel Statler	G Lim 300	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O	16	11/ 5/59 Fall 1960	11/ 6/59	C; 2 days	Unknown
#852—Ward Walks in Rare Diseases	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Los Angeles County Hospital	G Lim 15	II	BR, Lec	20	4/12/60	6/16/60	I; 10 sessions 2 hr. weekly, Tuesdays	100
Thirteenth Postgraduate Assembly	San Diego County General Hospital North end of Front St., San Diego 3, Calif.	S Lim 400	IC	BR, Sem, Lec, Pan, AV	12	11/ 4/59	11/ 5/59	C; 1½ days	Nil
A Series of Postgraduate Medical Programs	U.S. Veterans Administration Hospital (Fort Miley) 42nd Ave. and Clement St., San Francisco	G Lim 300	II	Lab, PD, LC, Sem, Lec, Pan, O	12	4/60	5/60	I; 6 sessions 2 hr. weekly, Tuesdays	15 AAGP members; 20 non-members; no fee interns and residents
New Drugs	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 100	IC	Lec, Pan, O, AV	15	Fall/59		C; 2 days	40
Medicine for General Practitioners	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco; course at Oakland Hospital, Oakland, Calif.	G Lim 50	II	Lec, O, AV	16	9/22/59	11/17/59	I; 8 sessions 2 hr. weekly, Tuesdays	35
Course for Physicians in General Practice	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco; course at Mt. Zion Hospital, San Francisco	G Lim 100	IC	Lab, PD, Clin C, Lec, Pan, O, AV	35	3/ 7/60	3/11/60	C; 5 days	80
Saint John's Hospital Postgraduate Assembly	John C. Eagan, M.D., Director Postgraduate Assembly, Saint John's Hospital 1328 22nd. St., Santa Monica, Calif.	G Lim 600	IC	Lab, LC, Clin C, Lec, Pan, O	28	9/10/59	9/12/59	C; 3 days	Nil

	course at Contra Costa County Hospital, Martinez, Calif.								
October Medical Clinics	Glockner-Penrose *Hospital* 2200 N. Tejon St., Colorado Springs, Colo. address after *October* 1, 2315 N. Cascade Ave., Colorado Springs	G	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	12	10/59		Unknown	10
General Practice Review	University of Colorado *School of* Medicine 4200 E. Ninth Ave., Denver 20	G	IC	Lec, Pan, O, AV	18	1/11/60	1/16/60	C; 6 days	55 or 10 per single day
Summer School of Alcohol Studies	Summer School of Alcohol Studies Yale University 52 Hillhouse Ave., Yale Station, New Haven, Conn.	G and non-medical persons	IC	PD, Sem, Lec, Pan, O, AV	74	6/60	7/60	C; 22 days	275
Management of Mass Casualties	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D.C.; course at Walter Reed Army Institute of Research, Washington 12, D.C.	S Lim 200	IC	Lec, Pan, O, AV, TV	44	9/14/59 2/15/60	9/19/59	C; 6 days	Nil
Management of Mass Casualties	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D.C.; course at Army Medical Service School Brooke Army Medical Center, Ft. Sam Houston, Tex.	G Lim 120	IC	Sem, Lec, Pan, O, AV		9/28/59 11/30/59 2/15/60 4/25/60 6/13/60	10/ 2/59	C; 5 days	Nil
Principles of *Medical* Operations in Nuclear Warfare	Department of the Army Office of the Surgeon *General* Personnel and Training Division Washington 25, D.C.; course at Walter Reed Army Institute of Research, Washington 12, D.C.	G (Military personnel only) Lim 24	IC	Lec, Pan, O, AV, TV		10/ 5/59	11/ 6/59	C; 25 days	Nil
Medico-Military Application Course for Nuclear Medical Officers	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D.C.; course at Walter Reed Army Institute of Research, Washington 12, D.C.	G (Military personnel only)	IC	Lec, Pan, O, AV, TV		3/21/60	4/22/60	C; 25 days	Nil
Advanced Orientation Course on Medical Aspects of Chemical Warfare	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D.C.; course at Army Chemical Center, Maryland	G (Military personnel only) Lim 30	IC	Lec, O, AV	21	5/ 5/60	5/ 9/60	C; 4 days	Nil
Seminar on Diabetes Mellitus	Dr. J. J. Lowenthal, President Florida Diabetes Association Marshall Taylor Bldg. Jacksonville, Fla.; course at The Balmoral Hotel, Miami Beach, Fla.	B	IC	Sem, Lec, Pan, O	10	10/29/59	10/30/59	C; 2 days	25
10th Annual Postgraduate Seminar—Recent Advances in Diagnosis and Therapy	Mount Sinai Hospital of Greater Miami 4300 Alton Rd., Miami Beach, Fla.	B Lim 800	IC	Sem, Lec, Pan, O, AV	20	5/12/60	5/14/60	C; 3 days	20
Medicine for Today—Gynecology, Surgery, Medicine, Eye, Ear, Nose and Throat	Illinois Academy of General Practice 14 E. Jackson Blvd., Chicago 4; course at Belleville, Centralia, Chicago (North), Chicago (South), Effingham, Geneva, Herrin, Hinsdale, Moline, Mount Carmel, Oak Park, Ottawa, Rockford, Waukegan	G	CC	Lec, O, AV	24	9/21/59 3/28/60	10/30/59	4 or 12 sessions 2 or 6 hr. each	50 members; 90 nonmembers
Asthma, Hay Fever and Allied Diseases	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Lec, O, EPP	140	1st Monday each mo.	Last Saturday of 4th wk.	24 days	200
Proctoscopy and Sigmoidoscopy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 5	IC	Lab, PD, LC, Lec, O, EPP	13	10/12/59 11/16/59 2/ 1/60 3/ 7/60 4/25/60 6/13/60	10/16/59	C; 5 days	100
General Medicine and Surgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.; course at Moila Temple, St. Joseph, Mo.	G	II	Lec, O, AV	9	9/15/59	5/17/60	I; 9 sessions 1 hr. monthly, Tuesdays	Nil
Infectious Diseases	University of Kansas Medical Center 39th and Rainbow Blvd , Kansas City, Ks.	G	IC	Lec, Pan, O, AV	7	9/25/59	9/25/59	C; 1 day	Nil
General Medicine and Surgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.; course at Southeast Kansas Tuberculosis Hospital, Chanute, Ks.	G	II	Lec, O, AV	6	11/17/59	4/19/60	I; 6 sessions 1 hr. monthly, Tuesdays	15

Key will be found on page 1938.

GENERAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
General Practice Symposia	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	H	PD, LC, Sem, Lec, Pan, O, AV	24	11/19/59	4/21/60	I; 6 sessions 4 hr. monthly, Thursdays	20
Kansas Circuit Course	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.; courses at Riley Hospital, Manhattan, Ks. St. Joseph Hospital, Concordia, Ks. Grace Hospital, Hutchinson, Ks. Colby Country Club, Colby, Ks. William Newton Memorial Hospital, Winfield, Ks. Hadley Memorial Hospital, Hays, Ks. Newman Memorial Hospital, Emporia, Ks. Trinity Hospital, Dodge City, Ks.	G	CC	PD, Sem, Lec, Pan, O, AV	33 at each location	12/ 1/59 12/ 1/59 12/ 2/59 12/ 2/59 12/ 3/59 12/ 3/59 12/ 4/59 12/ 4/59	4/26/60	5½ hr. one day a mo.; afternoon and evening for 6 mo.	30
The Ophthalmoscope: Its Use in Medicine	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, Lec, Pan, O, AV, EPP	7	2/11/60	2/11/60	C; 1 day	15
Medical-Surgical Subspecialties Symposia	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Sem, Lec, Pan, O, AV, TV	35	3/21/60	3/25/60	C; 5 days	80; 20 for single day
Fourth Annual Fall Clinical Conference on Coronary Artery Disease, Diabetes, Pulmonary Disease, Rheumatism	Lexington Clinic 1221 S. Broadway, Lexington, Ky.	G	IC	PD, Clin C, Sem, Lec, Pan, O, AV	11	10/21/59	10/22/59	C; 2 days	Nil
Second Norton Memorial Infirmary Post-Graduate Medical Seminar—Diseases of Calcification and Miscellaneous	Norton Memorial Infirmary 231 W. Oak St., Louisville 7, Ky.	G Lim 150	IC	Sem, Lec, O, AV	6	12/17/59	12/17/59	C; 1 day	Nil
Cancer Detection for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G Lim 2	IC	PD, EPP	12	continuous	2 days later	C; 2 days	5
Refresher Course for Physicians	Louisiana State University School of Medicine 1542 Tulane Ave., New Orleans 12; course at Confederate Memorial Hospital, Shreveport, La.	G Lim 125	H	Lab, PD, LC, Clin C, Pan, O, AV	54	9/59	5/60	I; 9 sessions 6 hr. monthly, Wednesdays	Unknown
Tri-State Medical Assembly	Dr. J. W. Wilson, Jr., Secretary Tri-State Medical Assembly 910 Margaret Place, Shreveport, La.; course at Confederate Memorial Medical Center, Shreveport, La.	G	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	8	10/ 2/59	10/ 3/59	C; 1½ days	10
Symposium on the Spine	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston	G Lim 100	IC	PD, Lec, O	12	10/23/59 Spring/60	10/24/59	C; 2 days	50
Postgraduate Course in General Medicine	St. Vincent Hospital 25 Winthrop St., Worcester 10, Mass.	G	H	PD, LC, Clin C	24	10/59	5/60	I; 16 sessions 1½ hr. twice monthly, Fridays	Nil
General Practice Circuit Course	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.; course at Alpena, Mich. Battle Creek, Mich. Bay City, Mich. Cadillac, Mich. Jackson, Mich. Lansing, Mich. Muskegon, Mich. Niles, Mich. Roscommon, Mich. Escanaba, Mich. Menominee, Mich. Iron Mountain, Mich. Sault Ste. Marie, Mich. Ironwood, Mich. Calumet, Mich. Marquette, Mich.	G	CC	PD, LC, Lec, Pan, O, AV		10/59 5/21/60 5/ 5/60 5/20/60 5/ 7/60 4/21/60 5/19/60 5/22/60 5/ 6/60 4/23/60 5/19/60 5/20/60 5/21/60 5/22/60 5/19/60 5/20/60 5/21/60	5/60	C; 2 days in each center, one in spring, one in fall	Unknown
Rheumatology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	Lab, PD, Clin C, Lec, O, AV	18	3/ 2/60	3/ 4/60	C; 3 days	10
Recent Advances in Therapeutics	University of Michigan Medical School								

Trauma for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O	7	3/10/60	3/19/60	C; 1 day	...
Circuit Courses	University of Mississippi Medical Center Public Information Department 2500 N. State St., Jackson, Miss.; course at North Mississippi Community Hospital, Tupelo, Miss., Greenwood Leflore Hospital, Greenwood, Miss. Memorial Hospital, Gulfport, Miss. Methodist Hospital, Hattiesburg, Miss. Matty Hersee Hospital, Meridian, Miss. University Medical Center, Jackson, Miss.	G	CC	Lec, Pan, O, AV	12	10/28/59 10/29/59 1/13/60 1/14/60 3/ 9/60 3/10/60	11/19/59	I; weekly 4 days each location	Nil
Fifth Annual Trauma Day	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	BR, Clin C, Sem, Lec, Pan, O, AV	6	5/ 4/60	5/ 4/60	C; 1 day	10
Newer Concepts in Medicine, Pediatrics, Obstetrics	Seton Hall College of Medicine and and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Monmouth Medical Center, Long Branch, N. J.	G Lim 45	II	PD, Clin C, Lec, O, AV	15	9/29/59	12/ 8/59	I; 10 sessions 1½ hr. weekly, Tuesdays	50
Recent Advances in Medicine and Surgery	Seton Hall College of Medicine and and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Peter's General Hospital, New Brunswick, N. J.	G Lim 40	II	PD, Clin C, Lec, Pan, O	15	9/29/59	12/ 8/59	I; 10 sessions 1½ hr. weekly, Tuesdays	50
One Day Seminar Obstetrics and Gynecology (A.M.) and General Surgery (P.M.)	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at The William McKinley Memorial Hospital, Trenton, N. J.	G Lim 40	IC	Sem, Lec, Pan, O, AV	8	Spring/60		C; 1 day	Unknown
Clinical Refresher Course—Choice of Subject	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 1	IC	PD, LC, BR	Arranged	Arranged		Arranged	60 for each five days
Two-Way Radio Conferences—Albany Medical College to Area Hospitals	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	O	Lec, O, R	23	11/ 9/59	4/29/60	I; 23 sessions 1 hr. weekly	Nil
Recent Advances in Clinical Practice	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV	39	9/14/59	9/19/59	C; 6 days	75
Minor Surgery and Office Orthopedics	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	10/14/59	10/15/59	C; 2 days	30
Arthritis	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	3/ 2/60	3/ 3/60	C; 2 days	30
Medicine PM 81—Arthritis	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Hospital for Joint Diseases, New York 35	G	IC	Lab, LC, Lec, O, AV	16½	10/22/59 4/22/60	10/24/59	C; 3 days	100
Postgraduate Radio Program—FM 93.9 megs	New York Academy of Medicine 2 E. 103rd St., New York 24	G	O	Lec, Pan, R	52	9/59	9/60	I; 1 hr. weekly, Thursdays	Nil
Postgraduate Week—Research Contributions to Clinical Practice	New York Academy of Medicine 2 E. 103rd St., New York 24	G	O	Lec, Pan	18	10/ 5/59	10/ 9/59	I; 10 sessions 1¾ hr.	Nil
Monthly Panel Meetings on Therapeutics for the General Physician	New York Academy of Medicine 2 E. 103rd St., New York 24	G	II	Lec	9	11/13/59	4/ 8/60	I; 1½ hr. monthly, Fridays	Nil
Anesthesiology—Diagnostic and Therapeutic Nerve Blocks	New York Medical College Metropolitan Medical Center Fifth Ave. at 106th St., New York 29	G	IC	PD, Sem, Lec, AV, EPP	45	Arranged		C; 5 days	125
Comprehensive Course in Medicine, Surgery, Allied Subjects	New York Polyclinic Hospital 345 W. 50th St., New York 19	B Lim 120	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, O, AV, TV	1260	9/59	6/60	C; 180 days	800
Evening Courses for the General Practitioner	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 20	II	PD, Lec	15	4/ 1/60 10/ 1/60		I; 8 sessions 1½ hr. days unknown	55
747—General Medicine. The Application of Recent Advances to Clinical Practice	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	II	Clin C, Lec, O, AV	64	9/22/59	5/17/60	I; 32 sessions 2 hr. weekly, Tuesdays	300
542—Review Course in General Medicine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	70	7/ 6/60	7/17/60	C; 10 days	125

Key will be found on page 1938.

GENERAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P. O. Box 1020, Chapel Hill, N. C.; course at Memorial Mission Hospital (Buncombe County) Asheville, N. C. Grace Hospital (Burke County) Morganton, N. C. Hotel Joseph Hewes (First District) Edenton, N. C. Undecided (Halifax-Nash-Edgecombe) Rocky Mount and Roanoke Rapids, N. C.	G	CC	Lec, Pan, O, AV	18 each location	9/15/59 9/16/59 1/13/60 1/14/60	10/27/59	I; 6 sessions 3 hr. weekly each location	25 each location
17th Annual Medical and Surgical Symposium of Watts Hospital	Watts Hospital Broad Street and Club Boulevard, Durham, N. C.	G	IC	PD, Clin C, Sem, Lec, Pan, O, AV	10	2/10/60 Usually similar date annually.	2/11/60	C; 2 days	Unknown
General Medicine	Frank E. Bunts Educational Institute 2020 E. 93rd St., Cleveland, Ohio	G Lim 125	IC	LC, Sem, Lec, Pan, O, AV	10	2/10/60	2/11/60	C; 2 days	20
Selected Topics in Medicine—10 Subjects (Pediatrics, Surgery, Eye, Ear Nose and Throat, etc.) presented	Registrar, Western Reserve University School of Medicine 2109 Adelbert Rd., Cleveland 6	G Lim 85	II	PD, Clin C, Sem, Lec, Pan, O, AV, TV	30	9/16/59	11/18/59	I; 10 sessions 3 hr. weekly, Wednesdays	30
Postgraduate Course in Clinical Medicine	Altoona Hospital Howard Ave., Altoona, Pa.	G	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	50	April, May/60		I; 6-10 sessions 6 hr. weekly, Thursdays	Unknown
Recent Advances in Medicine	St. Vincent Hospital 232 W. 25th St., Erie, Pa.	G	II	PD, LC, BR, Clin C, Lec, Pan, O, AV	21	10/ 7/59	11/18/59	I; 7 sessions 3 hr. weekly, Wednesdays	35
M.S.S.P. Hospital Training Course in Advances in Clinical Medicine	Commission on Graduate Education Medical Society State of Pennsylvania 230 State St., Harrisburg, Pa.; course at Pennsylvania Hospital, Philadelphia	G Lim 21	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	70	1/ 7/60	3/10/60	I; 10 sessions 7 hr. weekly, Thursdays	Unknown
General Hospital Course for General Practitioners	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 18	II	PD, LC, BR, Sem, Pan, AV, EPP	60	9/16/59	12/ 2/59	I; 12 sessions 5 hr. weekly, Wednesdays	75
Medical Writing	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	B Lim 20	II	Sem, Lec, Pan, O, AV, EPP	28	2/17/60	5/25/60	I; 14 sessions 2 hr. weekly, Wednesdays	50
Graduate Symposium on Geriatric Medicine	American Geriatrics Society 2907 Post Rd., Warwick, R. I.	G	IC	PD, Lec, Pan, O, AV	16	11/ 5/59	11/ 6/59	C; 2 days	Nil
Post Graduate Seminar and Founder's Day	Medical College of South Carolina 16 Lucas St., Charleston, S. C.	G	IC	PD, Sem, Lec, AV	22	11/ 4/59	11/ 6/59	C; 3 days	Nil
Greenville Post-Graduate Seminar	Greenville General Hospital 100 Mallard St., Greenville, S. C.	G Lim 300	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	22	4/60	4/60	C; 3 days	Nil
A Series of Advanced Clinical Bedside Courses—16 fields	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Texas Medical Center Institutions, Houston, Tex.	G Lim 5	II	Lab, PD, LC, BR, Sem, Lec, O, AV, EPP	8	9/ 1/59 1/ 5/60	9/22/59	I; 4 sessions 2 hr. weekly, Tuesdays	15
General Medicine	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Robert B. Green Memorial Hospital, San Antonio, Tex.	G Lim 75	IC	Lec, O, AV	6	10/18/59	10/18/59	C; 1 day	10
4th Annual Clinical Conference (Tumors of the Head and Neck)	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.	B Lim 200	IC	Lec, AV	9	11/13/59	11/14/59	C; 2 days	Unknown
Conference in Medicine and Surgery	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Scott and White Memorial Hospital, Temple, Tex.	G Lim 65	IC	Lec, Pan, O, AV	27	3/ 7/60	3/ 9/60	C; 3 days	5
Hill Country Summer Medical Seminars	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Villa Camillo, Hunt, Tex.	G	IC	Lec, O, AV	12	7/60	7/60	C; 3 days	50
Eighth Postgraduate Conference in Medicine and Surgery	University of Texas Postgraduate School of Medicine 213 W. Avenue G, Temple, Tex.; course at Scott and White Memorial Hospital; Scott, Sherwood and Brindley Foundation, Temple, Tex.	G	IC	Lab, PD, LC, Clin C, Sem, Surg Lec, Pan, O, AV	20	3/ 7/60	3/ 9/60	C; 3 days	25

	1400 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Tex.								
Newer Concepts in Medicine, Surgery, Obstetrics, and Gynecology	Mount Sinai Hospital 948 N. 12th St., Milwaukee	G Lim 200	II	Sem, Lec, O, AV	32	10/ 7/59 4/60	10/15/59	I; 4 sessions Wednesdays and Thursdays of 2 wk.	25

GYNECOLOGY

(See also Obstetrics and Gynecology, Pathology)

Course II—Gynecology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 18	IC	Lab, PD, LC, BR, Surg, O, AV, EPP	94	9/28/59 10/19/59 2/60 3/60 4/60 6/60	10/ 9/59	C; 11 days	150
Vaginal Approach to Pelvic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 16	IC	Lab, PD, LC, BR, Surg, Lec, O	20	10/12/59 11/16/59 2/ 1/60 3/ 7/60 4/25/60 6/13/60	10/16/59	C; 5 days	125
Gynecology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, Lec, Pan, O, AV	18	11/ 2/59	11/ 4/59	C; 3 days	45
Gynecology 3	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston	G Lim 50	IC	Lab, PD, LC, BR, Clin C, Lec	78	9/14/59	9/25/59	C; 11 days	175
Gynecology 4	Harvard Medical School 25 Shattuck St., Boston; course at Free Hospital for Women, Brookline, Mass.	G Lim 45	IC	Lab, PD, Clin C, Surg, Lec, Pan	45	4/25/60	4/29/60	C; 5 days	100
Gynecology for General Physicians	Continuation Medical Education 1312 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	18	6/13/60	6/15/60	C; 3 days	40
Clinical Gynecology	Department of Postgraduate Medical Education Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at St. Michael's Hospital, Newark, N. J.	Unknown	II	Unknown	Unknown	9/16/59	10/28/59	I; Wednesdays	25
Gynecology	University of Buffalo School of Medicine 3435 Main St., Buffalo	G Lim 16	IC	PD, Sem, Lec, Pan, O, AV	14	9/30/59	10/ 1/59	C; 2 days	30
Office Gynecology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Hospital of Brooklyn	G Lim 20	II	Lec, O	10	10/59	11/59	I; 10 sessions 1 hr. twice weekly Mondays, Fridays	20
561—Gynecological Cytology (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 6	II	Lab, Sem, Lec, O, AV, EPP	32	9/29/59 4/12/60	11/26/59	I; 16 sessions 2 hr. twice weekly, Tuesdays, Thursdays	100
560—Diagnosis and Therapy of Malignant Neoplasms of the Female Genital Tract	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 8	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, O, AV, EPP	35	10/ 5/59	10/ 9/59	C; 5 days	150
563—Gynecological Endocrinology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	Lab, PD, LC, Clin C, Sem, Lec, O	35	10/12/59 4/ 4/60	10/16/59	C; 5 days	140
562—Culdoscopy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 4	II	PD, LC, Surg, Lec, O, AV	6	11/16/59 4/25/60	11/20/59	I; 3 sessions 2 hr. thrice one week, Monday, Wednesday, Friday	55
Clinical Gynecology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	B	II	Lec, EPP	48	9/ 1/59 10/ 6/59 11/ 3/59 12/ 1/59	9/24/59	I; 8 sessions 6 hr. twice weekly, Tuesdays, Thursdays	50

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HEMATOLOGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Hematology	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	12	11/59		C; 2 days	To be determined
Clinical Hematology	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	S Lim 12	IC	Lab, Lec, EPP	40	6/60	6/60	C; 5 days	100
Hematology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Sem, Lec, O	40	6/60	5 days later	C; 5 days	100
Hematology—I	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	AV	15	10/26/59 4/25/60	6/27/60	9 monthly lessons	45
Clinical Traineeship in Hematology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	Lab, BR, Clin C, Lec, O, AV, EPP	120	11/ 1/59 2/ 1/60 3/ 1/60	11/30/59	C; 30 days	50 mo. Kansas residents; 100 mo. non-residents
Hematology—II	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	AV	15	11/ 3/59	7/ 5/60	9 monthly lessons	45
Hematology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	Lab, PD, Clin C, Lec, O, AV	35	2/22/60	2/26/60	C; 5 days	35
Hematology	Tufts University School of Medicine 136 Harrison Ave., Boston course at New England Center Hospital 171 Harrison Ave., Boston	G Lim 50	IC	PD, BR, Clin C, Sem, Lec, Pan, O, AV	14	4/ 7/60	4/ 9/60	C; 2 days	30
Medicine PM 66—Clinical Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 20	II	Lab, PD, BR, Lec, O, AV, EPP	72	9/ 8/59	1/19/60	I; 18 sessions 4 hr. weekly, Tuesdays	100
Medicine PM 20—Clinical Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	II	PD, LC, Lec, O, AV	24	10/27/59	12/15/59	I; 8 sessions 3 hr. weekly, Tuesdays	50
Medicine PM 67—Advanced Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 10	II	Lab, PD, EPP	37½	2/ 9/60	5/24/60	I; 15 sessions 2½ hr. weekly, Tuesdays	100
Medicine PM 21—Laboratory Methods in Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G Lim 6	IC	Lab, O, EPP	64	2/15/60	3/10/60	C; 16 days	200
Medicine PM 22—Laboratory Methods in Blood Banks	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S Lim 6	II	Lab, Sem, Lec	24	3/29/60	5/ 3/60	I; 6 sessions 4 hr. weekly, Tuesdays	50
Clinical Hematology—Diagnosis and Treatment of Blood Disorders	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York; course at Metropolitan Hospital, New York	G Lim 12	II	Lab, PD, BR, Lec	24	8/ 5/60	10/23/60	I; 8 sessions 3 hr. weekly, Mondays	75
541—Hematology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, Lec, Pan, O, AV	35	11/ 9/59	11/13/59	C; 5 days	90
544—Hematology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, LC, Lec, Pan, O	32	3/ 8/60	4/28/60	I; 16 sessions 2 hr. twice weekly, Tuesdays, Thursdays	55
Morphological Hematology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	G	II	Lec, O, AV	12	9/ 2/59	11/18/59	I; 12 sessions 1 hr. weekly, Wednesdays	25
Diseases of the Blood	Marquette University School of Medicine 8700 W. Wisconsin Ave., Milwaukee; course at Milwaukee County General Hospital, Milwaukee	G Lim 100	II	PD, LC, Lec, O	12	3/ 3/60	3/24/60	I; 4 sessions 3 hr. weekly, Thursdays	30

INTERNAL MEDICINE

(See also Basic Sciences, Cardiovascular Disease, Chest Diseases, Electrocardiography, Hematology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship and Special Skills Course—Medicine	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown

	University of California Medical Center Los Angeles 24								
855—*Intensive Review of Internal Medicine*	University of Southern California School of Medicine *Postgraduate Division* 2025 Zonal Ave., Los Angeles 33	G Lim 100	IC	Lec, O, AV	*40*	9/21/59	10/ 2/59	C; 10 days	65
852—Bedside Clinics in Internal Medicine	University of Southern California School of Medicine *Postgraduate Division* 2025 Zonal Ave., Los Angeles; course at Los Angeles County Hospital	B Lim 75	H	PD, LC, BR, Lec, Pan, O	24	10/ 8/59	1/11/60	I; 12 sessions 2 hr. weekly, Thursdays	65
842—Fundoscopy in Internal Medicine	University of Southern California School of *Medicine Postgraduate Division* 2025 Zonal Ave., Los Angeles 33; course at Los Angeles County Hospital	G Lim 30	H	LC, BR, Lec, Pan	12	4/ 5/60	6/14/60	I; 6 *sessions* 2 hr. weekly	37.50
Internal Medicine—A Selective Review	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 200	IC	PD, Clin C, Lec, Pan, O, AV	35	9/12/59	9/16/59	C; 5 days	20 per day
Liver Disease	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 75	IC	PD, Clin C, Lec, Pan, O, AV	14	10/59		C; 2 days	40
Laboratory Studies	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	B Lim 100	IC	PD, Lec, Pan, O, AV	18	11/ 5/59	11/ 7/59	C; 3 days	50
Arthritis	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 75	IC	PD, Lec, Pan, O, AV	14	Spring/60		C; 2 days	40
Present Concepts in Internal Medicine	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D. C. course at Letterman Army Hospital San Francisco	G Lim 100	IC	Lab, LC, Sem, Lec, Pan, O, AV	40	11/ 2/59	11/ 6/59	C; 5 days	Nil
Selected Topics in Internal Medicine	Georgetown University Medical Center 3800 Reservoir Rd., N.W. Washington, D. C.	S Lim 100	IC	PD, LC, Clin C, Lec, Pan, O, AV	30	9/28/59	10/ 2/59	C; 5 days	30 members Am. Coll. Phys.; 60 non-*members*
Professor Pro Tempore in Medicine	Mount Sinai Hospital of Greater Miami 1300 Alton Rd., Miami Beach, Fla.	G Lim 150	IC	PD, LC, BR, Clin C, Lec, Pan, O	18	11/59	5 days later	C; 5 days	Nil
Infectious Disease, Pulmonary Disease, Neurology, Gastroenterology, Cardiology, Hematology, Endocrinology, Renal Disease	Emory University *School of Medicine* 69 Butler St., S.E., Atlanta, Ga.	G Lim 60	IC	PD, Clin C, Sem, Lec, Pan, O, AV	40	9/28/59	10/ 2/59	C; 5 days	80
Electrolytes	Medical College of Georgia Augusta Ga.	G Lim 20	IC	PD, LC, Clin C, Sem, Lec, Pan	16	10/13/59	10/15/59	C; 3 days	25
Internal Medicine for the Internist—Part I	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 160	IC	Lec, AV	60	9/14/59 Spring/60	9/19/59	C; 6 days	125
Internal Medicine for the Internist—Part II	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 40	IC	PD, BR	48	9/28/59 Spring/60	10/ 3/59	C; 6 days	125
Course II in Internal Medicine—General Review	Cook County Graduate School of Medicine 707 S. Wood St., *Chicago 12*	G *Lim 30*	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	80	10/19/59 5/60	10/30/59	C; 11 days	150
Pulmonary *Function*	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	14	1/ 6/60	1/ 7/60	C; 2 days	20
Internal Medicine—Fluid and Electrolytes	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	1/20/60	1/20/60	C; 1 day	10
Weight Reduction and General Dietary Therapy	Indiana University School of *Medicine* 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	1/21/60	1/21/60	C; 1 day	10
Internal Medicine	University of Kansas *Medical Center* 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	28	11/16/59	11/19/59	C; 4 days	60
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Unknown Lim 2	PT	PT	Full time	Arranged	1 week or more later		25 per week
Topics in Clinical Medicine	Johns Hopkins Hospital 601 N. Broadway, Baltimore	G Lim 150	IC	PD, LC, Clin C, Sem, Lec, Pan, O	40	5/60		C; 5½ days	125
Diabetes Mellitus in Relation to General Medicine	Harvard Medical School 25 Shattuck St., Boston; course at New England Deaconess Hospital, Boston 15	G Lim 50	IC	PD, LC, BR, Clin C, Sem, Lec, O, AV	22½	10/ 5/59	10/ 7/59	C; 3 days	30
Recent Advances in Internal Medicine	Harvard Medical School 25 Shattuck St., Boston; course at Peter Bent Brigham Hospital, Boston 15	S *Lim 125*	IC	Lab, Clin C, Sem, Lec, Pan, O	38	6/ 6/60	6/11/60	C; 6 days	150

Key will be found on page 1933.

INTERNAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Internal Medicine 3	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston	G Lim 35	IC	PD, LC, Clin C, Lec	132	6/20/60	7/15/60	C; 22 days	300
A Review of Recent Advances in Internal Medicine	Tufts University School of Medicine 136 Harrison Ave., Boston; course at New England Center Hospital 171 Harrison Ave., Boston	G Lim 100	IC	PD, LC, Clin C, Sem, Lec, Pan, O	40	10/ 5/59	10/10/59	C; 5½ days	60
The Measurement of Pulmonary Function in Health and Disease	Edward J. Welch, M.D., Chairman 1101 Beacon St., Brookline, Mass.; course at Boston City Hospital	S Lim 150	IC	PD, Clin C, Sem, Lec, Pan, O, AV	35	3/21/60	3/25/60	C; 5 days	75
Internal Medicine	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S	IC or PT	Sem, Lec, O, AV	72	9/ 8/59	6/14/60	C; 36 evenings Tuesdays	50
Clinical Internal Medicine	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	II	PD, Clin C, Lec, O, AV	70	10/ 1/59	3/ 3/60	I; 3½ hr. weekly, Thursdays	65
Endocrinology and Metabolism	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, O, AV	30	4/11/60	4/15/60	C; 5 days	50
Medical Seminars	Highland Park General Hospital 369 Glendale Ave., Highland Park, Mich.	B	II	PD, LC, Clin C, Sem, Lec, O, AV	90	9/59	6/60	I; 42-44 sessions 2 hr. weekly, Wednesdays	Unknown
Internal Medicine for Internists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	3/14/60	3/16/60	C; 3 days	40
Diabetes	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	Clin C, Sem, Lec, Pan, O, AV	6	2/24/60	2/24/60	C; 1 day	10
Renal Diseases	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	PD, BR, Clin C, Sem, Pan, O, AV	12	2/25/60	2/26/60	C; 2 days	20
Recent Advances in Internal Medicine and Endocrinology	St. Michael's Hospital 306 High St., Newark, N. J.	G Lim 60	II	PD, LC, BR, Clin C, Lec, O, AV	24	9/59	3/60	I; 10 sessions 2 hr. every 2 weeks, Wednesdays	30
Recent Advances in Internal Medicine and Therapeutics	Middlesex General Hospital 180 Somerset St., New Brunswick, N. J.	G Lim 60	II	Sem, Lec, O, AV	70	9/23/59	6/22/60	I; 35 sessions 2 hr. weekly, Wednesdays	100; interns and residents of outside hospitals 25
One Day Seminar on Endocrinology, Gastroenterology, General Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Francis Hospital, Trenton, N. J.	G Lim 45	IC	Sem, Lec, Pan, O, AV	8	Fall/59	same day	C; 1 day	Unknown
Clinical Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Joseph Hospital, Paterson, N. J.	G Lim 50	II	PD, Clin C, Lec, O, AV	15	1/19/60	3/22/60	I; 10 sessions 1½ hr. weekly, Tuesdays	50
One Day Seminar on Endocrine and Liver Dysfunctions	Department of Postgraduate Medical Education Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at Elizabeth General Hospital, Elizabeth, N. J.	G Lim 40	IC	Sem, Lec, Pan, O, AV	8	Spring/60		C; 1 day	Unknown
Evaluation of Newer Drugs	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	3/23/60	3/24/60	C; 2 days	30
Special Teaching Day in Medicine	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	Sem, Lec, Pan, O, AV	5	11/12/59	11/12/59	C; 1 day	12
Diabetes and Basic Metabolic Problems	American Diabetes Association, Inc. 1 East 45th St., New York 17; course at The Ambassador, Los Angeles	G Lim 250	IC	PD, Clin C, Sem, Lec, Pan, O, AV	20	1/20/60	1/22/60	C; 3 days	40 members; 75 nonmembers
Management of Diabetes Mellitus	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Chronic Disease Hospital, Brooklyn, N. Y.	G Lim 20	II	PD, Lec	8	10/59	11/59	I; 8 sessions 1 hr. weekly, Thursdays	20
Recent Advances in Internal Medicine	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.;	G Lim 30	II	Lec, O	15	10/59	12/59	I; 10 sessions 1½ hr. weekly,	30

Medicine PM [illegible]	and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67								
Medicine PM 51—Chemotherapy of Infections and Parasitic Diseases	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	II	Lab, PD, LC, Lec, Pan, O, AV	9	10/20/59 3/ 1/60	11/ 5/59	I; 6 sessions 1½ hr. twice weekly, Tuesdays, Thursdays	50
Medicine PM 50—Diseases of the Liver	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	IC	PD, BR, Lec, O, AV	5 days	10/26/59	10/30/59	C; 5 days	100
Medicine PM 49—Management of Diseases of Metabolism for Internists	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S Lim 25	IC	PD, Clin C, Lec, Pan	21	11/12/59	11/14/59	C; 3 days	50
Salt and Water Metabolism	New York Heart Association Scientific Sessions Committee 10 Columbus Circle, New York; course at Hotel Biltmore New York	B	IC	Sem	16	12/11/59	12/12/59	C; 2 days	Nil
University of North Carolina School of Medicine Symposium on Metabolic and Endocrine Diseases	University of North Carolina School of Medicine North Carolina Memorial Hospital Box 1020, Chapel Hill, N. C.	G	IC	PD, BR, Clin C, Lec, Pan, O, AV	12	11/19/59	11/20/59	C; 2 days	Nil
New Concepts of Metabolic Disorders	Dr. Glenn W. Pfister, Jr., Secretary Southwestern Ohio Society of General Physicians—Educational Committee 1710 Section Rd., Cincinnati 37; course at University of Cincinnati College of Medicine, Cincinnati	G	IC	Sem, Pan	5	1/17/60	1/17/60	C; 1 day	10
Selected Topics in Internal Medicine—2 Afternoons Devoted to Each of 4 "Branches" of Internal Medicine as Hematology: Iron Deficiency Anemia and Hemolysis	Registrar, Western Reserve University School of Medicine 2109 Adelbert Rd., Cleveland 6	S Lim 85	II	PD, Clin C, Sem, Lec, Pan, O, AV, TV	28	3/23/60	5/11/60	I; 8 sessions 3½ hr. weekly, Wednesdays	35
Fourth Annual Sessions on Current Concepts in Rheumatic Diseases	Ohio State University, College of Medicine 11th and Neil Aves., Columbus 10, Ohio	G Lim 500	IC	PD, Clin C, Sem, Lec, Pan, O, AV	6½ hrs.	10/18/59	10/18/59	C; 1 day	5
Recent Advances in Metabolic Diseases	American College of Physicians 4200 Pine St., Philadelphia 4; course at Mount Sinai Hospital, New York	S	IC	Lec, O	35-40	Unknown			60 members; 80 nonmembers
Internal Medicine	American College of Physicians 4200 Pine St., Philadelphia 4; course at Georgetown University School of Medicine, Washington, D. C.	S	IO	PD, Lec, O	35-40	9/28/59	10/ 3/59	C; 5½ days	60 members; 80 non-members
Selected Subjects in Internal Medicine	American College of Physicians 4200 Pine St., Philadelphia 4; course at University of Buffalo School of Medicine, Buffalo	S Lim 100	IC	PD, Lec, O	15-35	10/ 5/59	10/ 8/59	C; 4 days	60 members; 80 non-members
Rheumatic Diseases	American College of Physicians 4200 Pine St., Philadelphia 4; course at Cornell University Medical College and New York Hospital, New York	S	IC	PD, Lec, O	35-40	1/11/60	1/15/60	C; 5 days	60 members; 80 non-members
Internal Medicine	American College of Physicians 4200 Pine St., Philadelphia 4; course at Henry Ford Hospital, Detroit	S	IC	PD, Lec, O	35-40	1/25/60	1/29/60	C; 5 days	60 members; 80 non-members
Pharmacotherapy	American College of Physicians 4200 Pine St., Philadelphia 4; course at University of Washington School of Medicine, Seattle	S	IC	PD, Lec, O	35-40	3/21/60	3/25/60	C; 5 days	60 A.C.P. members; 80 non-members
Internal Medicine—8 Subjects in Blocks of 1 to 4 Weeks	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at St. Joseph's Hospital Houston, Tex.	G	II	Sem, Lec, O, AV	48	1/ 5/60	5/17/60	I; 24 sessions 2 hr. weekly, Tuesdays	75
Fluid and Electrolyte Balance	University of Washington School of Medicine Seattle, Wash.	B Lim 10	IC	Lab, PD, Sem, Lec, O, AV, EPP	22½	9/23/59	9/26/59	C; 4 days	Unknown

MALIGNANT DISEASE

(See also Gynecology, Radiology, Radioisotopes, Pathology)

Cancer Symposium	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	3/30/60	3/30/60	C; 1 day	Nil

Key will be found on page 1938.

MALIGNANT DISEASE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Cancer Teaching Clinic	Westfield State Sanatorium Westfield, Mass.	G Lim 125	C	PD, Sem, Lec, Pan, O, AV	3	10/59 1/60 another topic	10/59	C; 1 day	Nil
Cancer Seminar	University of Mississippi Medical Center 2500 N. State St., Jackson, Miss.	G Lim 200	IC	Clin C, Sem, Lec, Pan, O, AV	7	12/ 3/59	12/ 3/59	C; 1 day	Unknown
Cancer	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV	7	12/10/59	12/10/59	C; 1 day	15
Cancer of the Head and Neck	Mary Imogene Bassett Hospital Cooperstown, N. Y.	G	IC	PD, Sem, Lec, Pan, O, AV	4	Not determined		C; 1 day	Unknown
Symposium on Evaluation of Early Diagnosis of Cancer	American Cancer Society, Inc., 521 W. 57th St., New York 19; course at Biltmore Hotel, New York	B	IC	Lec, Pan	12	10/26/59	10/27/59	C; 2 days	Nil
Medicine PM 72	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	II	PD, BR, Clin C, Sem, Lec, O, AV	140	9/ 9/59 1/ 6/60	1/27/60	I; 20 sessions 7 hr. weekly, Wednesdays	150
Diagnosis and Management of Early Cancer	Sloan-Kettering Institute Memorial and James Ewing Hospitals 444 E. 68th St., New York 21	G Lim 20	IC	PD, LC, Sem, Lec, O, AV	32	10/ 5/59	10/ 8/59	C; 4 days	50
Chemotherapy of Cancer	Sloan-Kettering Institute Memorial and James Ewing Hospitals 444 E. 68th St., New York 21	S Lim 25	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	60	10/26/59	11/ 6/59	C; 11 days	25

NEUROLOGY

(See also Basic Sciences, Electrocardiography, Surgery)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship and Special Skills Course—Neurology	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
13th Connecticut Postgraduate Seminar in Psychiatry and Neurology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S	II	Lec, O, AV	81	9/23/59	12/ 2/60	I; 4 hr. twice weekly	Nil
Seminar in Internal Medicine	University of Florida College of Medicine Gainesville, Fla.	B	IC	PD, Clin C, Sem, Lec, Pan, O	15	9/24/59	9/26/59	C; 2½ days	25
Medical-Surgical Symposia—Part IV. Neurology and Neurosurgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	O	PD, LC, Sem, Lec, Pan, O, AV	7	3/24/60	3/24/60	C; 1 day	20
Neurological Medicine	Harvard Medical School 25 Shattuck St., Boston; course at Boston City Hospital, Boston 15	S Lim 20	IC	Lab, PD, Lec	38	6/ 6/60	6/11/60	C; 6 days	150
Neurology	Tufts University School of Medicine 136 Harrison Ave., Boston; course at New England Center Hospital 171 Harrison Ave., Boston	G Lim 30	IC	PD, Lec, AV	22	4/27/60	4/30/60	C; 3 days	30
Clinical Neurology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, O, AV	18	4/18/60	4/20/60	C; 3 days	40
Pediatric Neurology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	30	2/15/60	2/19/60	C; 5 days	65
Clinical Neurology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Mountainside Hospital Montclair, N.J.	G Lim 50	II	Lec, O, AV	15	9/23/59	12/ 2/59	I; 10 sessions 1½ hr. weekly, Wednesdays	50
Neurology PM 33—Clinical Electroencephalography	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	II	Lab, Clin C, Lec, O	45	9/24/59	1/21/60	I; 15 sessions 3 hr. weekly, Thursdays	100
Neurology PM 30—Clinical Neurology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G Lim 20	IC	PD, LC, Sem, Lec, O, AV	30	3/28/60	4/ 1/60	C; 5 days	75
Neurology PM 61, Sect I & II, Advanced	Columbia University College of Physicians	S	IC	PD, LC, Sem, O, EPP	155	9/21/59	12/18/59	C; 65 days	150

Cerebral Palsy PM 1—A Postgraduate Course in Cerebral Palsy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	G	IC	LC, Lec, Pan, O, AV	105	[illegible]	[illegible]		
Advanced Functional Neuroanatomy—The Neuroanatomical Basis for Clinical Neurology	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G Lim 25	II	Lec	22	2/11/60	4/28/60	I; 11 sessions 2 hr. weekly, Thursdays	100
611—Electroencephalography	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 6	IC	Lab	Arranged	Arranged		Arranged	375
553—For the General Practitioner: Acute Problems of Central Nervous System	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, BR, Clin C, Surg, AV	35	10/12/59 4/25/60 6/20/60	10/16/59	C; 5 days	125
Review in Neurology	Manhattan State Hospital, Wards Island, New York; course at Goldwater Memorial Hospital Welfare Island, New York 17	S Lim 24	II	Lab, PD, Lec	115	9/16/59	12/ 9/59	I; 50 sessions 2 to 3 hr. 4 times weekly, Tuesdays, Wednesdays, Fridays, Sundays	175
Neurological Problems in Childhood—Acute Diseases	University of Washington School of Medicine Seattle, Wash.	S Lim 24	IC	Lab, PD, LC, BR, Sem, Lec, O, AV		10/59			Unknown

NEUROLOGY AND PSYCHIATRY

(See also each category)

Psychiatry PM 1—Psychiatry and Neurology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at New York State Psychiatric Institute, New York	S	PT	Lab, PD, LC, Clin C, Sem, Lec	400	10/ 5/59	12/11/59	50 days, Full time	300
643—Neurology and Psychiatry	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	IC	PD, LC, Lec	420	9/14/59	12/ 4/59	C; 12 weeks	325
716—Basic Psychiatry and Neurology	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Lec	22½	10/ 2/59 2/12/60	1/22/60	I; 15 sessions 1½ hr. weekly, Fridays	60
Refresher Course in Psychiatry and Neurology	The University Health Center Columbus 10, Ohio; course at Ohio State University College of Medicine Department of Psychiatry, and the Columbus Psychiatric Institute and Hospital, Columbus 10	S Lim 8	IC	PD, BR, Clin C, Sem, Lec, O, AV, EPP	120	11/ 2/59	11/25/59	C; 20 days	300

OBSTETRICS

Obstetrical Complications	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 200	IC	Clin C, Sem, Lec, O, AV	18	9/17/59	9/19/59	C; 3 days	50
Course I—Obstetrics	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 14	IC	Lab, PD, LC, BR, Surg, Lec, O, AV	75	9/14/59 11/ 2/59 2/60 3/60 5/60	9/25/59	C; 11 days	150
Clinical Obstetrics	Harvard Medical School 25 Shattuck St., Boston; course at Boston Lying-in Hospital, Boston	G Lim 6	IC	PD, LC, BR, Clin C	120-130	10/ 1/59 11/ 1/59 4/ 1/60 5/ 1/60	10/31/59	C; 27 days	150
Obstetrics for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	10/ 5/59	10/ 7/59	C; 3 days	40
Clinical Obstetrics (One Month Observation)	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N.J.; course at Margaret Hague Maternity Hospital, Jersey City, N.J.	G	PT	PD, LC, BR, Clin C, Lec, O, AV, EPP		1st of month arranged	1 mo. later	30 days	100
Clinical Obstetrics—Pre and Post Natal Care; Medical and Surgical Complications; Technics and Principles; etc.—Traineeship	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N.J.; course at Margaret Hague Maternity Hospital, Jersey City, N.J.	G	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	Full time	1st of month arranged	3 mo. later		350
Obstetrical Seminars	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Margaret Hague Maternity Hospital, Jersey City, N.J.	G Lim 40	II	Unknown	9	11/ 4/59	11/18/59	I; 3 sessions 3 hr. weekly, Wednesdays	30

ey will be found on page 1938.

OBSTETRICS—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Obstetrics	University of Buffalo School of Medicine 3435 Main St., Buffalo	G Lim 16	IC	PD, Sem, Lec, Pan, O, AV	14	2/24/60	2/25/60	C; 2 days	30
Operative Obstetrics (Manikin)	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 10	II	PD, LC, BR, Clin C, Lec, O, AV	21	Arranged		I; 6 sessions 2 hr. twice weekly, Wednesdays, Fridays	150
The Conduct of Labor and Delivery	Women's Hospital—Division of St. Luke's Hospital 111 W. 109th St., New York	G Lim 14	IC or PT	Lab, PD, LC, BR, Clin C, Lec, Pan, O, AV, EPP	35	10/ 8/59	10/11/59	C; 7 days	75

OBSTETRICS AND GYNECOLOGY

(See also Anatomy, Gynecology, Obstetrics, Pathology, Basic Sciences)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Summer Seminar on Obstetrics and Gynecology	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	S	IC	Sem, Lec, O, AV	21	7/11/60	7/13/60	C; 3 days	35
Armed Forces Seminar in Obstetrics and Gynecology	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D. C.	S (Military personnel only) Lim 100	IC	Lec, Pan, AV	40	5/ 2/60	5/ 6/60	C; 5 days	Nil
Seminar in Obstetrics and Gynecology—Recent Advances	University of Florida College of Medicine Gainesville, Fla.	B	IC	PD, Clin C, Sem, Lec, Pan, O	15	2/25/60	2/27/60	C; 2½ days	25
Obstetrics and Gynecology	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	11	3/ 2/60	3/ 3/60	C; 2 days	20
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Unknown Lim 2	PT	PT	Full time	Arranged	1 week or more later		25 per week
Obstetrics and Gynecology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, O, AV	18	1/27/60	1/29/60	C; 3 days	40
Obstetrics and Gynecology	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	Clin C, Sem, Lec, Pan, O, AV	12	1/21/60	1/22/60	C; 2 days	20
Obstetrics and Gynecology	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	Clin C, Sem, Lec, Pan, O, AV	6	3/31/60	3/31/60	C; 1 day	10
Obstetrics and Gynecology Traineeship	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G Lim 7	PT	PD, LC, BR, Clin C, Sem, Surg, Lec, EPP	40	6/20/60	6/25/60	5½ days	75
Clinical Obstetrics and Gynecology	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 35	II	PD, Clin C, O, AV	15	9/30/59	12/ 9/59	I; 10 sessions 1½ hr. weekly, Wednesdays	50
Special Teaching Day in Obstetrics and Gynecology	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	Sem, Lec, Pan, O, AV	5	1/21/60	1/21/60	C; 1 day	12
Recent Advances in Obstetrics and Gynecology	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	II	Sem, Lec, Pan, O, AV	14	2/25/60	3/17/60	I; 4 sessions 3½ hr. weekly, Thursdays	25
Culdoscopy	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 10	II	PD, Lec	6	4/ 1/60		I; 3 sessions 2 hr. Monday, Wednesday, Friday	100
Gynecology and Obstetrics Including Manikin Obstetrics and Operative Gynecology	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	136	4/ 1/60 10/ 1/60	4/30/60	C; 30 days	250
501—Infertility	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 16	IC	Lab, PD, Clin C, Surg, Lec, O, EPP	21	11/30/59	12/ 2/59	C; 3 days	50
Obstetrics-Gynecology Office Problems	Dr. Glenn W. Pfister, Jr., Secretary Southwestern Ohio Society of General Physicians—Educational Committee 1710 Section Rd., Cincinnati 37; course at Hartwell Country Club, Cincinnati	G	IC	Sem, Lec, Pan, O	5	11/15/59	11/15/59	C; 1 day	10
Obstetrics and Gynecology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Texas Medical Center, Houston, Tex.	G Lim 50	II	Lec, Pan, O, AV	9	6/ 7/60	6/21/60	I; 3 sessions 3 hr. weekly, Tuesdays	20
Clinical and Fundamental Aspects of Common Problems in Obstetrics and Gynecology	University of Washington School of Medicine Seattle, Wash.	G	IC	PD, Sem, Lec, O, AV		Spring/60			

OCCUPATIONAL MEDICINE

Aviation Medicine—Space Survival	Department of Continuing Education in *Medicine and Health Sciences* University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	18	10/28/59	10/30/59	C; 3 days	60
The Prevention and Management of Athletic Injuries	University of *Colorado School* of Medicine 1200 E. Ninth Ave., Denver 20	B	IC	Sem, Lec, Pan, O, AV	Undetermined	8/60	8/60	C; 3 days	Unknown
Occupational *Medicine*	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D.C.; course at United States *Army* Environmental Health Laboratory, Edgewood, Md.	S Lim 30	IC	Lec, Pan, O	10	10/12/59	10/16/59 5/ 2/60	C; 5 days	Nil
School Health	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	Sem, Lec, Pan, O, AV	7	10/ 1/59	10/ 1/59	C; 1 day	Nil
Institute on Occupational Hearing Loss	William A. Macomber, Director Division of *Adult Education* Colby College, Waterville, Me.	M.D., engineers, other	IC	Lab, Clin C, Lec, Pan, O, AV, EPP	36	8/17/59	8/21/59	C; 5 days	Unknown
Industrial Medicine and *Occupational* Health	Postgraduate Committee, University of Maryland School of Medicine 522 W. Lombard St., Baltimore	G Lim 100	II	Sem, Lec, Pan, O	12	10/ 1/60	10/ 8/60	I; 2 sessions 6 hr. weekly twice Thursdays	20
Newer Concepts in Industial Medicine	Seaton Hall *College* of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Mercer Hospital Trenton, N.J.	G Lim 45	II	Lec, O, AV	15	Fall/59		I; 10 sessions 1½ hr. each	25
Industrial Toxicology—Occupational Poisoning	Columbia University School of Public Health and Administrative Medicine 600 W. 168th St., New York 32	S	HS	HS		Any time			20
Occupational Medicine 202	Columbia University School of Public Health and Administrative Medicine 600 W. 168th Street, New York 32	G Lim 6	II	Clin C, Sem, Lec	24	2/ 1/60	3/25/60	I; 16 sessions 1½ hr. twice weekly; Mondays, Thursdays	37
Institute for Physicians in Industry —Statistics, Epidemiology, Toxicology	Columbia University School of Public Health and Administrative *Medicine* 600 W. 168th Street, New York 32	S	IC	Clin C, Sem, Lec, O	36	2/ 5/60	2/ 9/60	C; 5 days	108
Occupational Medicine 203—Industrial Medical Organization	Columbia University School of Public Health and Administrative Medicine 600 W. 168th Street, New York 32	G	II	Lec, O, AV	18	3/28/60	5/27/60	I; 9 sessions	37
Bureau of School Health Pre-Service Training Course for School Health Physicians	Dr. Robert W. Culbert, Director Department of Health 125 Worth St., New York 13; course at Kips Health Center, New York	G Lim 10	IC	Sem	90	Fall/59 Spring/60		C; 30 days	Nil
Bureau of Child Health Pre-Service Training Course for Physicians in Infant and Preschool Division	Dr. Harold Jacobziner, Assistant Commissioner, New York City Department of Health 125 Worth St., New York; course at Kips Bay Health Center, New York	G	IC	LC, Sem, Lec, O, AV	150	10/ 5/59	11/ 6/59	C; 30 days	Unknown
489—Special Topics in Industrial Hygiene Laboratory Methods	New York University Post-Graduate Medical School 550 First Ave., New York 16	B	II	Lab	Arranged	Arranged	Arranged	Arranged	Arranged
486—Industrial Hygiene	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-physicians Lim 30	II	Lab, Lec		9/59		I; 15 days	100
488—Chemical Methods in Industrial Hygiene	New York University *Post-Graduate* Medical School 550 First Ave., New York 16	G and non-physicians Lim 10	II	Lab, Lec, AV		9/59		I; 15 days	110
481—A. Occupational Medicine for Physicians	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	Sem, Lec, Pan, AV	280	9/14/59	11/ 6/59	C; 40 days	375 plus 25 Field Trip Expenses
482—Occupational Medicine for Physicians	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 50	II	PD, Clin C, Sem, Lec, AV	90	9/17/59	5/12/60	I; 30 sessions 3 hr weekly, Thursdays	300
483—Medical Aspects of Compensation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 100	IC	Sem, Lec, Pan, AV	35	10/19/59	10/23/59	C; 5 days	60
4810—Air Pollution	New York University *Post-Graduate* Medical School 550 First Ave., New York 16	G and non-physicians	IC	Lab, Lec, AV, EPP	70	11/30/59	12/11/59	C; 10 days	100

Key will be found on page 1938.

OCCUPATIONAL MEDICINE—Continued

Title of Co:	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
186-L—Industrial Hygiene Laboratory	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-physicians Lim 10	II	Lab, Lec, AV		2/60		I; 15 days	100
4811—Industrial Toxicology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-physicians Lim 20	II	Lab, Lec, AV		2/60		I; 15 days	110
Eye Care in Industry	Institute of Industrial Health Kettering Laboratory Eden and Bethesda Ave , Cincinnati 19	S Lim 50	IC	PD, Clin C, Sem, Lec, O	30	1/19/60	1/23/60	C; 5 days	100
Occupational Skin Problems	Institute of Industrial Health Kettering Laboratory Eden and Bethesda Ave , Cincinnati 19	G	IC	PD, Sem, Lec, Pan, O	40	10/26/59	10/30/59	C; 5 days	100
Postgraduate Course in Aviation Medicine	Ohio State University College of Medicine 10th and Neil Aves., Columbus, Ohio	G Lim 40	IC	LC, Sem, Lec, Pan, O, AV, EPP	40	9/14/59 9/60	9/18/59	C; 5 days	75

OPHTHALMOLOGY

(See also Basic Sciences)

Title of Co:	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Glaucoma	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 16	IC	PD, Lec, Pan, O, AV, EPP	14	Arranged		C; 2 days	60
Annual Ophthalmology Conference	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 100	IC	PD, LC, Lec, Pan, O, AV	24	12/ 2/59	12/ 5/59	C; 3½ days	Unknown
Ophthalmology	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	Lec, AV	Undetermined	7/60	7/60	C; Undetermined	Unknown
Ophthalmic Pathology	Armed Forces Institute of Pathology 6825 16th St., N.W., Washington 12, D. C.	S Lim 50	IC	Lab, Lec, AV	36	3/28/60	4/ 1/60	C; 5 days	Nil
Ophthalmology	Emory University School of Medicine 69 Butler St., S.E., Atlanta 3, Ga.	S	IC	Unknown	16	12/ 3/59	12/ 4/59	C; 2 days	Unknown
Clinical Ophthalmology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Surg	50	Arranged	2 wk. later	10 days	50
Extraocular Muscles I—Diagnosis and Treatment of Strabismus	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 5	IC	PD, LC, Sem, Lec	24	9/14/59	9/25/59	C; 10 days	100
Extraocular Muscles II— Diagnosis and Treatment of Strabismus	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 5	II	PD, LC, BR, Sem, Lec	200	Arranged		I; 100 sessions 2 hr. arranged	150
Clinical Traineeship in Ophthalmology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	S Lim 1	PT	Lab, BR, Clin C, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. nonresidents
Glaucoma	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	14	12/11/59	12/12/59	C; 2 days	50
Ophthalmology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	Clin C, Lec, Pan, O, AV	17	4/ 4/60	4/ 6/60	C; 3 days	40
The Lancaster Courses in Ophthalmology—Basic Science	Dr. Parker Heath, Director Ophthalmological Study Council, Sullivan Harbor, Me.; course at Colby College, Waterville, Me.	B Lim 80	IC	Lab, Clin C, Sem, Lec, Pan, O, EPP	445	6/20/60	9/ 5/60	C; 66 days	325
Ophthalmology	Harvard Medical School 25 Shattuck St., Boston; course at Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston	S Lim 30	IC	Lab, PD, Clin C, Lec	35-40 per week	9/28/59	3/11/60	C; 5 mo.	675
Ophthalmology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	S Lim 150	IC	Lec, O, AV	18	4/25/60	4/27/60	C; 3 days	50
Ophthalmology for Specialists	Continuation Medical Education 1342 Mayo Memorial, University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	1/11/60	1/13/60	C; 3 days	40
Home Study Course in Ophthalmology	American Academy of Ophthalmology and Otolaryngology 15 Second St., S.W., Rochester, Minn.	S	HS (C)	Assigned reading		9/ 1/59	6/30/60	9 mo.	20
Anatomy, Physiology, Pathology, Diagnosis and Treatment of Anomalies of Extraocular Muscles	United Hospitals of Newark—Eye and Ear Infirmary Unit 77 Central Ave., Newark, N. J.	S Lim 16	II	PD, LC, Clin C, Surg, Lec	8	10/22/59	11/12/59	I; 4 sessions 2 hr. weekly, Thursdays	Nil
Neuro-Ophthalmology—Intracranial Lesions Impinging on Ocular Cranial Nerves	United Hospitals of Newark—Eye and Ear Infirmary Unit	S Lim 16	II	PD, LC, BR, Clin C, Lec	8	11/19/59	12/17/59	I; 4 sessions 2 hr. weekly,	Nil

Corneal and Scleral Contact Lenses—Choice, Technic, and Fitting	*United Hospitals of Newark—Eye and Ear Infirmary Unit* 77 Central Ave., Newark, N. J.	S Lim 15	II	PD, LC, Clin C, Sem, Lec, O, EPP	8	1/ 7/60	1/28/60	I: 4 sessions 2 hr. weekly Thursdays	80
A Seminar on Glaucoma with Particular Emphasis on Gonioscopy	Brooklyn Eye and Ear Hospital 29 Greene Ave., Brooklyn, N. Y.	S Lim 6	IC	PD, LC, Lec, O, EPP	18	5/18/60	5/20/60	C: 3 days	50
Ophthalmology PM 31—Glaucoma	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	II	PD, Lec, O, AV, EPP	9	10/ 6/59	10/23/59	I: 6 sessions 1½ hr. twice weekly, Tuesdays Fridays	50
Ophthalmology PM 60—Elementary Ophthalmoscopy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	II	PD, Lec, O, AV, EPP	16	10/21/59	12/ 9/59	I: 8 sessions 2 hr. weekly, Wednesdays	20
Ophthalmology PM 32—Ophthalmoscopy for General Practitioners and Pediatricians	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G Lim 12	II	Lab, PD, Clin C, EPP	12	11/ 5/59	12/ 3/59	I: 8 sessions 1½ hr. twice weekly, Tuesdays, Thursdays	75
Ophthalmology PM 62—Glaucoma	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	II	PD, Sem, O, AV	18	1/ 6/60	3/ 2/60	I: 9 sessions 2 hr. weekly, Wednesdays	30
Ophthalmology PM 33—The Use of the Schepen's Ophthalmoscope	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 8	II	PD, Sem, EPP	12	3/ 8/60	3/24/60	I: 6 sessions 2 hr. twice weekly, Tuesdays, Thursdays	50
Ophthalmology PM 30—Histopathology of the Eye	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 10	II	Lab, Lec, O, EPP	16	4/ 6/60	4/29/60	I: 8 sessions 2 hr. weekly, Wednesdays, Fridays	100
Fundoscopy—The Use of the Ophthalmoscope	New York Medical College Flower and Fifth Ave., Hospitals Fifth Ave., and 106th St., New York; course at Metropolitan Hospital, New York	G Lim 5	II	LC, EPP	10	Arranged		I: 5 sessions 2 hr. weekly, Wednesdays	50
Plastic Eye Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 10	II	PD, LC, Surg, Lec, O, AV	12	9/14/59	10/ 1/59	I: 6 sessions 7 hr. twice weekly, Mondays, Thursdays	200
Recent Advances in Cataract Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, Pan, O, AV, TV	14	9/15/59	9/16/59	C: 2 days	75
Advances in Ocular Prostheses	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 10	II	PD, Lec, O, AV	4	9/16/59	9/23/59	I: 2 sessions Wednesdays	20
Glaucoma	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	IC	PD, Surg, Lec, O, AV, EPP	11	9/18/59	9/19/59	C: 2 days	75
Gonioscopy and Tonography	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 15	O	PD, Lec, O, AV, EPP	3	9/21/59 11/16/59		O: 1 day 1 day	15
Keratectomies and Keratoplasties	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 30	IC	Lab, PD, Surg, Lec, O, AV, TV, EPP	14	9/22/59	9/23/59	C: 2 days	75
Light Coagulation (Meyer-Schwickerath Apparatus)	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	IC	Lab, PD, Sem, Surg, O, AV, EPP	4	9/24/59	9/25/59	C: 2 days	20
Retinal Detachment	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 30	IC	PD, Surg, Lec, O, AV, EPP	14	9/25/59	9/26/59	C: 2 days	75
Pathology of the Eye	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 20	IC	Lab, Lec, O, AV	23	9/28/59 5/60	10/ 2/59	C: 5 days	100
Lacrimal Sac Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 15	IC	Lab, PD, Surg, Lec, O, AV, TV	7	9/29/59	9/29/59	C: 1 day	35
Surgery of the Orbit	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 10	IC	Lab, PD, LC, BR, Surg, Lec, O, AV, TV	7	9/30/59	9/30/59	C: 1 day	35
Enucleation and Evisceration	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	IC	PD, Surg, Lec, O, AV, TV	7	10/ 5/59	10/ 5/59	C: 1 day	35

Key will be found on page 1938.

OPHTHALMOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Anomalies of Extraocular Muscles, Including Ptosis	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 10	IC	PD, LC, Surg, Lec, O, AV, TV, EPP	19	10/ 5/59	10/ 9/59	C; 5 days	100
Fundamental Principles of Orthoptics	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 20	O	PD, LC, Lec, O	3	10/ 8/59	10/ 8/59	C; 1 day	15
Biomicroscopy, Biomicroscopy Using Near Ultra-Violet, Cobalt Blue and Polarized Light, and Gonioscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 20	IC	PD, LC, Lec, O, AV, EPP	14	10/ 9/59	10/10/59	C; 2 days	75
Biomicroscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 8	II	PD, LC, Lec, O, AV, EPP	16	10/19/59	11/11/59	I; 8 sessions 2 hr. twice weekly, Mondays, Wednesdays	80
Pleoptics and Macular Function Testing	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 10	II	PD, Lec, O, AV, EPP	4	10/19/59	10/21/59	I; 2 sessions 2 hr. twice weekly, Mondays, Wednesdays	20
Complications of Ophthalmologic Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 20	II	Lab Lec, O, AV	10	10/19/59	10/28/59	I; 5 sessions, 2 hr. thrice weekly, Mondays, Wednesdays, Fridays	50
Ocular Therapeutics	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 20	II	Lec, O, AV	16	10/20/59	11/12/59	I; 8 sessions 2 hr. twice weekly, Tuesdays, Thursdays	80
Ophthalmoscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 8	II	PD, LC, Lec, O, AV, EPP	16	10/20/59	11/12/59	I; 8 sessions 2 hr. twice weekly, Tuesdays, Thursdays	80
Refraction	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 25	II	PD, Lec, O, AV	12	10/20/59	11/ 5/59	I; 6 sessions 2 hr. twice weekly, Tuesdays Thursdays	60
Contact Lenses	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	II	PD, LC, Lec, O, AV, EPP	9	10/26/59	10/30/59	I; 3 sessions, 3 hr. thrice in one week, Monday, Wednesday, Friday	45
Ocular Biochemistry	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 8	IC	Lab, Lec, O, AV	7½	10/26/59	10/30/59	C; 5 days	35
Ocular Microbiology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 8	IC	Lab, Lec, O, AV, EPP	6	10/26/59	10/29/59	C; 4 days	30
Ocular Geriatrics	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 20	O	Lab, Lec, O, AV	2	10/30/59	10/30/59	C; 1 day	10
Ocular Photography	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 11	IC	Lec, O, AV, TV, EPP	7	10/31/59	10/31/59	C; 1 day	35
Perimetry	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S	II	PD, Lec, O, AV, EPP	8	11/ 2/59 5/60	11/ 6/59	I; 3 sessions, 2½hr. thrice in one week, Monday, Wednesday, Friday	40
Ocular Radiology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 9	IC	Lab, PD, LC, Lec, O, AV	6	11/ 2/59	11/ 5/59	C; 4 days	30
Ocular Neuro-Ophthalmology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S	II	PD, LC, Lec, O, AV	10	11/ 3/59	11/17/59	I; 5 sessions 2 hr. twice weekly, Tuesdays, Thursdays	50
Physiological Optics	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 15	II	Lec, O, AV, EPP	6	11/ 4/59	11/ 6/59	I; 2 sessions 3 hr. twice weekly, Wednesdays, Fridays	30
Biomicroscopy, Using Near Ultra-Violet, Cobalt Blue and Polarized Light	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	IC	PD, LC, Lec, O, AV, EPP	4	11/ 9/59	11/10/59	C; 2 days	20
Low Vision Aids	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 15	O	PD, LC, Lec, O, EPP	2	11/13/59	11/13/59	C; 1 day	10

Psychosomatic Factors in Ophthalmology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 15	IC	Lec, O, AV	3	11/15/59	11/15/59	C; 1 day	15
Radio-Isotopes in Ophthalmology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 12	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, O, AV, EPP	15	11/16/59	11/20/59	C; 5 days	75
Clinical Bacteriology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 8 for Lab	IC	Lab, Lec, O, AV, EPP	5	11/19/59	11/20/59	C; 2 days	25
Electrophysiology and Applied Physiology of the Eye	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 10	IC	Lab, PD, LC, Lec, O, AV, EPP	9	11/23/59	11/25/59	C; 3 days	45
Ophthalmic Plastic Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 8	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, TV, EPP	100	1/60		C; 15 days	250
Ocular Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York 3	S Lim 25	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, Pan, O, AV, TV	50	5/60	1 week later	C; 6 days	200
571—Ophthalmic Plastic Surgery (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 15	IC	PD, Surg, Lec, Pan, O, AV	15	11/16/59 3/14/60	11/20/59	C; 5 days	90
572—Surgery of the Cornea	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 10	IC	Lab, PD, LC, Surg, Lec, O, AV, TV, EPP	35	11/30/59	12/ 4/59	C; 5 days	250
573—Neuro-Ophthalmology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S	IC	PD, Lec, O, AV	15	1/18/60	1/22/60	C; 5 days	55
574—Motor Anomalies of the Eye (Part I) (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 25	IC	PD, Clin C, Lec, Pan, O, AV	12	2/29/60	3/ 5/60	C; 6 days	115
575—Motor Anomalies of the Eye (Part II) (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 16	IC	PD, LC, Clin C, Lec, Pan, O, AV, EPP	35	3/ 7/60	3/11/60	C; 5 days	100
576—Ocular Expressions of Systemic Disease	New York University Post-Graduate Medical School 550 First Ave., New York 16	S	IC	PD, Lec, Pan, O, AV	15	3/21/60	3/25/60	C; 5 days	60
578—Surgery of the Eye (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 11	IC	Lab, PD, LC, Surg, Lec, Pan, O, AV, EPP	12	3/28/60	4/ 2/60	C; 6 days	125
Ophthalmoscopy	New York University Post-Graduate Medical School 550 First Ave., New York 16	S	IC	PD, Lec, O, AV	15	4/25/60	4/29/60	C; 5 days	60
579—Histopathology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S	IC	Lab, Lec, O, AV	15	4/25/60	4/29/60	C; 5 days	100
Newer Developments in Ophthalmology	Frank E. Bunts Educational Institute 2020 E. 93rd St., Cleveland, Ohio	S Lim 125	IC	LC, Sem, Lec, Pan, O, AV	12	12/ 9/59	12/10/59	C; 2 days	25
Ophthalmology Postgraduate Conference	Ohio State University College of Medicine 11th and Neil Aves., Columbus 10, Ohio	S Lim 250	IC	Lec	14	3/ 7/60	3/ 8/60	C; 2 days	20
Postgraduate Convention—Ophthalmology	Secretary-Treasurer Oregon Academy of Ophthalmology and Otolaryngology Postgraduate Convention 1216 S. W. Yamhill St., Portland 5, Ore.; course at University of Oregon Medical School, Portland 1, Ore.	S	IC	Lec, Pan, O, AV	16	3/14/60	3/15/60	C; 2 days	60; or 90 if compined with Otolaryngology course
Biomicroscopy of the Posterior Vitreous and Fundus	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.	S and residents Lim 20	II	Lec, O, AV	3	12/ 2/59	12/16/59	I; 3 sessions 1 hr. weekly, Wednesdays	10
Ophthalmology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at Robert B. Green Memorial Hospital, San Antonio, Tex.	G	IC	Lec, AV	12	1/23/60	1/24/60	C; 2 days	25
OPHTHALMOLOGY AND OTOLARYNGOLOGY									
Postgraduate Convention—Ophthalmology and Otolaryngology	Secretary-Treasurer Oregon Academy of Ophthalmology and Otolaryngology Postgraduate Convention 1216 S.W. Yamhill St., Portland 5, Ore.; course at University of Oregon Medical School, Portland 1, Ore.	S	IC	Lec, Pan, O, AV	32	3/11/60	3/15/60	C; 4 days	90
Thirty-Third Annual Spring Congress in Ophthalmology and Otolaryngology	Gill Memorial Eye, Ear and Throat Hospital 711 S. Jefferson St., Roanoke, Va.	S Lim 200	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, O, AV, TV	40	4/ 4/60	4/ 9/60	C; 5½ days	80

Key will be found on page 1938.

ORTHOPEDIC SURGERY

(See also Anatomy, Basic Sciences)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Orthopedics—Surgery and Fractures	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco; course at Mt. Zion Hospital, San Francisco	G Lim 35	IC	PD, Lec, Pan, O, AV	14	9/59		C; 2 days	50
Management of Common Orthopedic Disorders in Children	Department of Continuing Medical Education in Medicine and Health Sciences University of California Medical School Second and Parnassus Ave., San Francisco 22; course at Children's Hospital, San Francisco	G Lim 100	IC	Lec, Pan, O, AV	7	1/23/60	1/23/60	C; 1 day	12.50
Instructional Course Program	American Academy of Orthopedic Surgeons 116 S. Michigan Ave., Chicago	G	IC	PD, Clin C, Sem, Lec, Pan, O, AV	9	1/24/60	1/27/60	C; 4 days	15
Orthopedics	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	PD, Lec, Pan, O, AV	7	2/17/60	2/17/60	C; 1 day	10
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Unknown Lim 2	PT	PT	Full time	Arranged	1 week or more later		25 per week
Surgery of the Hand	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	G Lim 50	IC	PD, Sem, Lec, Pan, O, AV	20	3/ 3/60	3/ 5/60	C; 2½ days	25
Orthopedic Surgery 1	Harvard Medical School 25 Shattuck St., Boston; course at Children's Hospital, Boston	S Lim 2	IC	Lab, PD, LC, BR, Sem, Surg, Lec	Variable	Arranged		C; Arranged	200 for 3 mo.
Orthopedic Surgery 2	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston	S Lim 2	IC	Lab, PD, LC, BR, Sem, Surg, Lec	Variable	Arranged		C; Arranged	800 for 12 mo.
Orthopedic Surgery PM 81—Foot Disabilities: a Survey of the Diagnostic and Therapeutic Problems of the Foot	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32 course at Hospital for Joint Diseases New York 35	S	IC	PD, Lec, O, AV	18	10/ 1/59	10/ 3/59	C; 3 days	100
Orthopedic Surgery PM 80	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32 course at Hospital for Joint Diseases New York 35	G	IC	PD, Lec, O, AV	36	10/12/59	10/17/59	C; 6 days	100
Orthopedic Surgery PM 1—Orthopedic Surgery, Musculoskeletal Disease & Injury	Columbia University College of Physicians and Surgeons 630 W 168th St., New York 32 course at Columbia-Presbyterian Medical Center, New York 32	S	IC	Lec, O, AV	35	11/ 9/59	11/13/59	C; 5 days	100
Basic Engineering for Orthopedic Surgeons	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	S Lim 10	II	PD, BR, Lec	12	Arranged		I; 12 sessions 1 hr. ea.	100
Orthopedics of the Foot	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	S Lim 5	II	PD, LC, BR, Surg, Lec	24	Arranged		I; 8 sessions, 3 hr. weekly, day by arrangement	100
581—Orthopedics for the General Practitioner	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, BR, O, AV, EPP	16	10/ 6/59	12/ 1/59	I; 8 sessions 2 hr. weekly, Tuesdays	45
582—Orthopedic Aspects of the Treatment of Rheumatic Disorders	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, BR, Clin C, Lec, O, AV	20	10/ 7/59	12/ 9/59	I; 10 sessions 2 hr. weekly, Wednesdays	50
584—Orthopedics in General Practice	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, BR, O, AV, EPP	21	2/17/60	2/19/60	C; 3 days	55
585—Orthopedic Aspects of the Treatment of Rheumatic Disorders	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, LC, BR, Clin C, Lec, O, AV	21	3/15/60	3/29/60	I; 3 sessions 7 hr. weekly, Tuesdays	50
Basic Science Conference for Orthopedic Surgeons	Ohio State University, College of Medicine 11th and Neil Aves., Columbus 10, Ohio	S	IC	Sem, Lec	16	3/ 9/60	3/10/60	C; 2 days	Unknown

OTOLARYNGOLOGY

(See also Anatomy, Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Ear, Nose and Throat	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	12	11/13/59	11/14/59	C; 2 days	50
Ear-Nose-Throat	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center	G Lim 10	IC	PD, LC, Lec, Pan, O, AV, EPP	14	Spring/60		C; 2 days	40

Clinical Otolaryngology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Surg, O	60	Arranged	2 wk. later	10 days	50
Fellowship Fenestration Surgery	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 2	IC	Lab, PD, LC, BR, Clin C, Sem, O, Lec	960	Arranged		C; 80 days	500
Basic Otologic Surgery	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 10	IC	Lab, PD, LC, BR, Clin C, Sem, Lec	200	2/ 1/60	3/ 4/60	C; 5 weeks	800
Annual Otolaryngologic Assembly—Current Trends in Otolaryngology	University of Illinois College of Medicine 1853 W. Polk St., Chicago 12	S Lim 40	IC	Lab, PD, Clin C, Sem, Lec, Pan, O, AV	75	9/18/59	9/26/59	C; 9 days	125
Bronchoesophagology	University of Illinois College of Medicine 1853 W. Polk St., Chicago 12	S 15	IC	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec, O, AV	84	11/ 9/59	11/21/59	C; 12 days	210
Anatomical and Clinical Otolaryngology	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	S	IC	Lab, PD, Lec, Pan, O, AV, EPP	100	4/ 4/60	4/16/60	C; 13 days	250
Clinical Traineeship in Otorhinolaryngology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S Lim 1	PT	Lab, BR, Clin C, Sem, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. non-residents
Otolaryngology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	Clin C, Lec, Pan, O, AV	17	4/ 6/60	4/ 8/60	C; 3 days	40
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Unknown Lim 2	PT	PT	Full time	Arranged	1 week or more later		25 per week
Otolaryngology for General Practitioners	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	G Lim 25	IC	Sem, Lec, Pan	16	4/21/60	4/22/60	C; 2 days	25
Otology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Lim 60	IC	Lec, O, AV	18	4/21/60	4/23/60	C; 3 days	50
Otolaryngology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	5/23/60	5/25/60	C; 3 days	40
Home Study Course in Otolaryngology	American Academy of Ophthalmology and Otolaryngology 15 Second St., S. W., Rochester, Minn.	S	HS(C)	Assigned reading		9/ 1/59	6/30/60	9 mo.	20
Otorhinolaryngology PM 30—Transmeatal (Endaural) Surgery	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 9	IC	Lab, Surg, Lec, O, AV, EPP	80	9/ 8/59 3/28/60	9/19/59	C; 10 days	350
Otorhinolaryngology PM 32—Combined Course in (a) Indirect Laryngoscopy and Voice Rehabilitation and (b) Audiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	IC	PD, LC, Sem	21 each section	2/ 8/60 (section a) 2/11/60 (section b)	2/10/60	C; 6 days, both sections	75 per section; 150 entire course
Otorhinolaryngology PM 31—Mobilization of Stapes	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 6	IC	Lab, PD, Surg	120	4/18/60	5/ 6/60	C; 15 days	500
Otorhinolaryngology PM 33—Rhinoplasty and Otoplasty	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 30	IC	Lab, LC, Surg, Lec, O, AV	112	7/16/60	7/29/60	C; 14 days	350
591—Endaural Surgery	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 8	IC	Lab, PD, Sem, Lec, Pan, O, AV, EPP	70	11/ 9/59 2/ 1/60	11/20/59	C; 10 days	275
595—Laryngology and Surgery of the Larynx and Neck	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 10	IC	Lab, PD, LC, Sem, Surg, Lec, Pan, O, AV, EPP	70	1/11/60	1/22/60	C; 10 days	250
592—Audiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 15	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV, EPP	21	2/29/60	3/ 2/60	C; 3 days	60
593—Neuro—Otology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 10	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	21	3/ 3/60	3/ 5/60	C; 3 days	50
Twenty-Fourth Annual Graduate Convention in Otology, Rhinology, and Laryngology—Regional Anatomy and Cadaver Surgery	University of Cincinnati College of Medicine Eden and Bethesda Aves., Cincinnati 19	S Lim 22	IC	Lab, PD, Clin C, Sem, Surg, Lec, O, AV, EPP	45	4/11/60	4/16/60	C; 5½ days	150
Postgraduate Convention—Otolaryngology	Secretary-Treasurer Oregon Academy of Ophthalmology and Otolaryngology Postgraduate Convention 1216 S. W. Yamhill St., Portland 5, Ore.; course at University of Oregon Medical School, Portland 1, Ore.	S	IC	Lec, Pan, O, AV	16	3/11/60	3/12/60	C; 2 days	60; or 90 if combined with Ophthalmology course

Key will be found on page 1938.

OTOLARYNGOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
ryngology and Laryngeal Surgery	Chevalier Jackson Clinic Temple University Medical Center 3401 N. Broad St., Philadelphia 40	B Lim 10	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, Pan, O, AV, EPP	80	9/14/59	9/25/59	C; 11 days	250
habilitation of the Laryngectomee	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	G also non-physicians	IC or II	PD, Lec, O, AV, EPP	70	6/60	6/60	C; 10 days	Unknown

PATHOLOGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
athology 200—Brain Tumor Registry —Neuropathology	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S Neurosurgery, Neurology, and Neuropathology	IC	Sem, O, AV	Arranged	Arranged		Arranged	Arranged
Application of Histochemistry to Pathology	Armed Forces Institute of Pathology 6825 16th St., N.W., Washington 12, D. C.	S Lim 30	IC	Lab, Sem, Lec	35	10/26/59	10/30/59	C; 5 days	Nil
Forensic Pathology	Armed Forces Institute of Pathology 6825 16th St., N.W., Washington 12, D. C.	S Lim 50	IC	Lab, Sem, Lec, Pan, O, AV, TV	35	11/ 8/59	11/13/59	C; 6 days	Nil
Pathology of Diseases of Laboratory Animals	Armed Forces Institute of Pathology 6825 16th St., N.W., Washington 12, D. C.	S Lim 60	IC	Lec	36	12/ 7/59	12/11/59	C; 5 days	Nil
Pathology of the Oral Regions	Armed Forces Institute of Pathology 6825 16th St., N.W., Washington 12, D. C.	B and dentists Lim 100	IC	Sem, Lec, Pan	35	3/14/60	3/18/60	C; 5 days	Nil
Ophthalmic Pathology	Armed Forces Institute of Pathology 6825 16th St., N.W., Washington 12, D. C.	S Lim 50	IC	Lab, Sem, Lec, AV	35	3/28/60	4/ 1/60	C; 5 days	Nil
Refresher Course for Laboratory Medical Officers	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D. C.	S (Military personnel only) Lim 20	IC	Lab, Sem, Lec, Pan, O, AV, EPP	44	2/ 8/60	2/13/60	C; 6 days	Nil
Cancer Cytology	Cancer Institute at Miami 1155 N. W. 14th St., Miami, Fla.	G	PT	Lab, PD, Sem, Lec, Pan, O, AV, EPP		Continuous	1 mo. to 1 yr. later		150 for 1st. mo. to 450 for 1 yr.
Surgical Pathology for Specialty Board Candidates	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 5	IC	Lab, Clin C, Lec, O, EPP	38 wk.	Arranged	2 or 4 wk. later	C; 6, 12, 18, or 24 days	150 to 250
Surgical Pathology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 9	IC	Lab, Clin C, Sem, Lec, O, EPP	48	Arranged	2 wk. later	C; 12 days	150
Surgical Pathology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 9	IC	Lab, Clin C, Sem, O, EPP	96	Arranged	4 wk. later	C; 24 days	250
Clinical Traineeship in Pathology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	Lab, Clin C, Sem, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. non-residents
Neuropathology	Postgraduate Committee, University of Maryland School of Medicine 522 W. Lombard St., Baltimore	S Lim 3	IC	Lab, Sem	Unknown	Arranged	6 mo. later	C; 6 mo.	210
Pathology of Obstetrics and Gynecology	Harvard Medical School 25 Shattuck St., Boston	S Lim 12	II	Lab, Lec	80	1/ 7/60	5/19/60	I; 20 sessions 4 hr. each	200
Pathology with Clinical Application	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Lim 10	IC or PT	Lab, PD, Clin C, Lec, O, AV	310	9/28/59	12/19/59	C; 60 days	250
Pathology GM 1—Surgical Pathology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	G	PT	Lab, PD, Clin C, EPP		1st day ea. mo. to July 1960		6 or 12 mo.	300 for 6 mo; 600 for 12 mo.
Pathology PM 31—Surgical	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	B Lim 12	II	Lab, Lec, O, AV	30	9/12/59	12/19/59	I; 15 sessions 2 hr. weekly, Saturdays	100
Pathology PM 30—General and Special Pathology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Lab, Lec, O, AV	30	9/19/59	12/26/59	I; 15 sessions 2 hr. weekly, Saturdays	100
al Pathology	Columbia University College of Physicians	S Lim 12	II	Lab, PD, Lec, O, AV	16	1/ 4/60	1/28/60	I; 8 sessions 2 hr. twice weekly Mondays,	100

Otolaryngology PM 2—Histopathology of the Ear, Nose and Throat	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32 course at Columbia-Presbyterian Medical Center, New York 32	S	II	Lab, Lec, AV, EPP	32	4/ 5/60	5/28/60	I; 16 sessions 2 hr. twice weekly, Tuesdays, Thursdays	100
Special Pathology—Gynecological and Surgical Pathology	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	S Lim 9	II	Lab, Lec, O, AV	90	Arranged		I; 30 sessions 3 hr. twice weekly, Tuesdays, Fridays	200
Gynecological and Obstetrical Pathology	New York Polyclinic Hospital 345 W. 50th St., New York 19	S Lim 8	IC	Lab, PD, LC, Clin C, Lec	15	Arranged		C; 10 days	50
Urological Pathology	New York Polyclinic Hospital 345 W. 50th St., New York 19	S Lim 8	IC	Lab, PD, Clin C, Lec	15	Arranged		C; 10 days	50
Surgical Pathology	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec	50	4/ 1/60 10/ 1/60	4/30/60	C; 24 days	50
532—Toxicology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-physicians Lim 6	IC	Lab, Sem, Lec, AV, EPP		Arranged		Arranged	100 per mo.
Gynecological Pathology—Correlation of Pathologic Findings with Clinical Diagnosis	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex. course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	B Lim 4	II	Lab, Lec	8	9/ 1/59 10/ 6/59 11/ 3/59 12/ 1/59	9/24/59	I; 8 sessions 1 hr. twice weekly, Tuesdays, Thursdays	10
Pathologic Anatomy and Pathology of Human Tumors	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex. course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	G and residents	II	Lec	26	10/ 7/59	3/30/60	I; 26 sessions 1 hr. weekly, Wednesdays	30
General Oncology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex. course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	G	II	Lec	12	11/25/59	2/10/60	I; 12 sessions 1 hr. weekly, Wednesdays	25
Dermatopathology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex. course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	G and residents Lim 20	II	Lec, AV	17	3/ 1/60	6/21/60	I; 17 sessions 1 hr. weekly, Tuesdays	30

PEDIATRICS

(See also Allergy, Neurology, Surgery, Psychiatry)

Clinical Traineeship and Special Skills Course—Pediatrics	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
Fever	Department of Continuing Medical Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco course at Children's Hospital, San Francisco	G Lim 100	IC	Lec, Pan, O, AV	7	3/19/60	3/19/60	C; 1 day	12.50
Clinical and Research Advances in Pediatrics and Child Guidance Problems	University of Colorado School of Medicine 1200 E. Ninth Ave., Denver 20 course at Stanley Hotel, Estes Park, Colorado	S Lim 200	IC	Sem, Lec, Pan, O, AV	36	9/ 3/59	9/ 8/59	C; 4½ days	60; or 35 for each part
Pediatric Postgraduate Day	University of Colorado School of Medicine 1200 E. Ninth Ave., Denver 20	B	II	PD, LC, Sem, Lec, Pan, O, AV	36	10/ 2/59	5/ 6/60	I; 9 sessions 4 hr. first Friday each month	Nil
13th Connecticut Postgraduate Seminar in Psychiatry and Neurology—Pediatric Neurology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S	II	Lec, O	16	2/15/60	4/ 4/60	I; 2 hr. weekly	Nil
Seminar in Pediatrics—Recent Advances	University of Florida College of Medicine Gainesville, Fla.	B	IC	PD, Clin C, Sem, Lec, Pan, O	15	2/11/60	2/13/60	C; 2½ days	25
Pediatrics	American Academy of Pediatrics 1801 Hinman Ave., Evanston, Ill.; course at Tulane University School of Medicine, New Orleans	S Lim 70	IC	PD, Clin C, Lec, Pan, O, AV	21	2/10/60	2/12/60	C; 3 days	40
Problems of the Newborn	American Academy of Pediatrics 1801 Hinman Ave., Evanston, Ill.; course at Ohio State University College of Medicine, Columbus Children's Hospital, Columbus, O.	S Lim 70	IC	PD, Clin C, Lec, Pan, O, AV	21	3/23/60	3/25/60	C; 3 days	40

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PEDIATRICS—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Pediatric Cardiology	American Academy of Pediatrics 1801 Hinman Ave., Evanston, Ill.; course at University of Minnesota Graduate School of Medicine, Rochester, Minn.	S Lim 70	IC	PD, Clin C, Lec, Pan, O, AV	21	3/30/60	4/ 1/60	C; 3 days	40
Problems in Diagnosis and Treatment	American Academy of Pediatrics 1801 Hinman Ave., Evanston, Ill.; course at Children's Hospital, Washington, D. C.	S Lim 70	IC	PD, Clin C, Lec, Pan, O, AV	21	5/18/60	5/20/60	C; 3 days	40
General Pediatrics	American Academy of Pediatrics 1801 Hinman Ave., Evanston, Ill.; course at Tulane University School of *Medicine, New Orleans*	S Lim 50	IC	Unknown	28	2/10/60	2/13/60	C; 3½ days	60 members; 70 non-members
Clinical Pediatrics	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Sem, O, EPP	60	Arranged	2 wk. later	12 days	60
Clinical Pediatrics	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Sem, O, EPP	120	Arranged	4 wk. later	12 days	100
Course V—Pediatrics	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 25	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	70	4/18/60	4/29/60	C; 10 days	150
The Neuromuscular Diseases of Children with Special Emphasis on Cerebral Palsy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 30	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	80	6/13/60	6/24/60	C; 11 days	250
Pediatrics	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	12/ 9/59	12/ 9/59	C; 1 day	10
Clinical Traineeship in Pediatrics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Lab, BR, Clin C, Sem, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; *100 mo. non-residents*
Pediatrics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Clin C, Lec, Pan, O, AV	21	3/ 7/60	3/ 9/60	C; 3 days	15
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Lim 2	PT	PT	Full time	Arranged	1 wk. or more later		25 per wk.
Pediatric Postgraduate Course	Department of Pediatrics, University of Louisville School of Medicine 323 E. Chestnut St., Louisville 2; course at Children's Hospital, Louisville 2	G Lim 50	II	PD, LC, Clin C, Lec, O	24	4/12/60	5/31/60	I; 8 sessions 3 hr. weekly, Tuesdays	30
Pediatrics 2	Harvard Medical School 25 Shattuck St., Boston; course at Children's Hospital, Boston 15	G Lim 8	IC	Lab, PD, LC, BR, Clin C, Lec, Pan, O	30 hr. per week	10/ 1/59 2/ 1/60	1/23/60	C; 14 weeks	500
Pediatrics 3	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston 14	G Lim 50	IC	PD, Clin C, Lec	70	6/ 6/60	6/17/60	C; 11 days	150
Pediatric Metabolism and Endocrinology	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston 14	G	IC	PD, Lec	28	6/14/60	6/17/60	C; 4 days	70
Pediatrics	Tufts University School of Medicine *136 Harrison Ave., Boston;* course at New England Center Hospital 171 Harrison Ave., Boston	G *Lim 10*	IC	PD, Clin C, Lec, Pan, O	14	3/17/60	3/19/60	C; 2 days	30
Pediatrics	University of Michigan Medical School Department of Postgraduate Medicine *University Hospital, Ann Arbor, Mich.*	G Lim 10	IC	PD, Clin C, Lec, Pan, O, AV	18	1/25/60	1/27/60	C; 3 days	40
Prevention and Management of Handicapping Conditions in Infancy and Childhood	University of Michigan School of Public Health Ann Arbor, Mich.	G and others *Lim 100*	IC	Sem, Lec, Pan, O	40	11/16/59	11/20/59	C; 5 days	Nil
Pediatrics for Pediatricians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	9/22/59	9/24/59	C; 3 days	40
Pediatrics for General Physicians	Continuation Medical Education *1342 Mayo Memorial* University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	15	2/29/60	3/ 2/60	C; 3 days	40
Pediatrics	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	PD, Clin C, Sem, Lec, Pan, O, AV	12	4/ 4/60	4/ 5/60	C; 2 days	20
Current Practical Thinking About Common Pediatric Problems	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.	G Lim 10	II	PD, Clin C, Lec, Pan, O, AV	15	9/30/59	12/ 9/59	I; 10 sessions 1½ hr. weekly Wednesdays	50
Pediatric Teaching Day	Albany Medical College	G	IC	Sem, Lec, Pan, O	5	12/ 3/59	12/ 3/59	C; 1 day	12

Course in Clinical Pediatrics	Albany Medical College 17 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	BR, Clin C, Sem, O	21	3/24/60	4/28/60	I; 6 sessions 3½ hr. weekly, Thursdays	30
610—*Pediatric Endocrinology and Related Metabolism*	*New York* University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, Clin C, Lec, AV	24	11/ 9/59	11/12/59	C; 4 days	90
612—Seminar on General Pediatrics	New York *University Post-Graduate* Medical School 550 First Ave., New York 16	G	II	LC, Clin C, Sem, Lec, Pan, AV	36	9/30/59	5/25/60	I; 18 sessions 2 hr. weekly, Wednesdays	125
Postgraduate Symposium in Advances in Pediatrics	Rochester Regional Hospital Council 154 East Ave., Rochester, N. Y.; course at University of Rochester Medical Center, Rochester, N. Y.	B	IC	LC, Clin C, Sem, Lec, O, AV	15	10/14/59	10/16/59	C; 3 days	45
The Letchworth Village Graduate Course in Mental Retardation	Research Foundation for Mental Hygiene, Inc. Letchworth Village, Thiells, N. Y.	B Lim 700	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, AV, EPP	120	9/14/59 10/19/59 3/14/60 4/18/60	10/ 3/59	C; 18 days	Nil
Seminar on Pediatrics	Dr. Glenn W. Pfister, Jr., Secretary Southwestern Ohio Society of General Physicians—Educational Committee 1710 Section Rd., Cincinnati 37; course at University of Cincinnati College of Medicine, Cincinnati	G	IC	Sem, Pan, O	5	3/13/60	3/13/60	C; 1 day	10
Pediatrics for the General Practitioner	Hahnemann Medical College and Hospital 230 N. Broad St., *Philadelphia* 2	G Lim 25	II	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	24	9/23/59	12/ 9/59	I; 12 sessions 2 hr. weekly, Wednesdays	50
General Pediatrics	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at Scott and White Memorial Hospital, Temple, Tex.	G Lim 2	IC	PD, LC, BR, Sem, Surg, O	176	9/ 7/59	10/ 3/59	C; 24 days	25
Pediatrics	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at Turner Home, El Paso, Tex.	G Lim 60	IC	Lec, Pan, O, AV	7	2/ 7/60	2/ 7/60	C; 1 day	10
Postgraduate Refresher Course in Pediatrics	University of Texas Postgraduate School of Medicine 213 W. Avenue G, Temple, Tex.; course at Scott and White Memorial Hospital; Scott, Sherwood and Brindley Foundation, Temple, Tex.	G Lim 1	IC	PD, LC, BR, EPP	176	1/60 First Monday of mo.	12/60 Last Saturday of mo.	C; 24 days	25
Pediatric Allergy and Recent Advances in Care of Newborn Infants	University of Washington School of Medicine Seattle, Wash.	S Lim 24	IC	PD, LC, BR, Clin C, Sem, Lec, O, AV		9/17/59	9/19/59	C; 3 days	Unknown
Pediatric Diagnosis and Treatment	*Marquette University* School of Medicine 8700 W. Wisconsin Ave., Milwaukee; course at Milwaukee Children's Hospital, Milwaukee	G Lim 100	II	PD, LC, Lec, O	12	4/ 6/60	4/27/60	I; 4 sessions 3 hr. weekly, Wednesdays	30

PERIPHERAL VASCULAR DISEASE

Treatment of Varicose Veins	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 12	IC	Lab, PD, LC, Surg, Lec, O	10	9/14/59 10/26/59 11/ 7/59 12/ 7/59 Offered 9 times during 1960	9/16/59	C; 2 days	50
Femoral Arteriography and Aortography	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	IC	Lab, PD, LC, BR, Surg, Lec, O, EPP	12	9/15/59 12/ 8/59 6 starting dates in 1960	9/18/59	C; 4 days	100
Medicine PM 65	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 15	II	PD, Sem, Lec, O, AV, EPP	63	11/ 5/59	4/ 7/60	I; 21 sessions 3 hr. weekly, Thursdays	100
Medicine PM 65A—Advanced Course in Peripheral Vascular Surgery	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 15	II	PD, Sem, Lec, O, AV	54	11/18/59	3/30/60	I; 18 sessions 3 hr. weekly, Wednesdays	150
Peripheral Vascular Diseases	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Coney Island Hospital, Brooklyn, N. Y.	G Lim 20	II	Lec	10	10/59	12/59	I; 10 sessions 1 hr. weekly, Mondays	20

Key will be found on page 1938.

PERIPHERAL VASCULAR DISEASE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Principles and Treatment of Peripheral Vascular Diseases	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York; course at Metropolitan Hospital, New York	G Lim 15	H	PD, Sem, Lec	18	9/14/59 3/60	1/11/60	I; 12 sessions 1½ hr. weekly, Mondays	150
Seminar in Peripheral Vascular Disease	Dr. Hilmer W. Neumann 1124 Carew Tower, Cincinnati; course at University of Cincinnati College of Medicine *Good Samaritan Hospital, Cincinnati*	B	IC	Sem, Lec, O, AV	14	10/14/59	10/15/59	C; 2 days	15

PHYSICAL MEDICINE AND REHABILITATION

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship and Special Skills Course—Physical Medicine and Rehabilitation	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
Physical Medicine	Department of Continuing *Education in* Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	PD, Lec, Pan, O	14	9/59		C; 2 days	40
Fundamentals of Physical Medicine and Rehabilitation	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	H	PD, Lec	Undetermined	1/60	3/60	I; weekly day unknown	Unknown
Physical Medicine and Rehabilitation	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	Lec, AV	Undetermined	5/60	5/60	C; Undetermined	Unknown
Physical Therapy and Occupational Therapy in the Care of Neuro-Muscular Disease	Georgia Warm Springs Foundation Warm Springs, Ga.	G Lim 35	IC	PD, LC, Lec, Pan, O	36	9/28/59 1/ 4/60 3/28/60	10/ 2/59	C; 5 days	Nil
Physical Therapy and Occupational Therapy in the Care of Neuro-Muscular Disease	Georgia Warm Springs Foundation Warm Springs, Ga.	G Lim 18	IC	PD, LC, Lec, Pan, O, AV, EPP	180	9/28/59 1/ 4/60 3/28/60	12/18/59	C; 90 days	Nil
Physical Therapy and Occupational Therapy in the Care of Neuro-Muscular Disease	Georgia Warm Springs Foundation Warm Springs, Ga.	G Lim 18	IC	PD, LC, Lec, Pan, O, AV, EPP	960	9/28/59 1/ 4/60 3/28/60	3/26/60	C; 180 days	Nil
Clinical Traineeship in Physical Medicine	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	BR, Clin C, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. non-residents
Technics of Physical Rehabilitation	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, Lec, O, AV	7	10/16/59	10/16/59	C; 1 day	5
Physical Medicine for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	PD, Lec, Pan, O, AV	15	11/19/59	11/21/59	C; 3 days	40
Physical Medicine and Rehabilitation GM 1	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	G Lim 3	PT	PD, Clin C, AV		1st day ea. mo. to July 1960		6 or 12 mo.	300 for 6 mo.; 600 for 12 mo.
Annual Scientific Seminar of American Academy of Physical Medicine and Rehabilitation	Joseph Benton, M.D., Chairman, Program Committee, State University of New York 450 Clarkson Ave., Brooklyn 3, N. Y.; *course at Hotel Leamington, Minneapolis*	G	IC	Clin C, Sem, Lec, Pan	14	8/31/59	9/ 1/59	C; 2 days	Nil
Physical Medicine and Rehabilitation in Clinical Practice	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV, EPP	14	12/ 2/59	12/ 3/59	C; 2 days	30
Rehabilitation Care of the Chronically Ill Patient	Department of Physical Medicine and Rehabilitation, New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	B and others	IC	Unknown	Unknown	11/16/59	11/20/59	C; 5 days	100
621—Physical Medicine and Rehabilitation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, Lec	70	10/12/59	10/23/59	C; 10 days	110
Physical Medicine and Rehabilitation	Highland View Hospital 3901 Ireland Drive, Cleveland 22	G Lim 10	IC	PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	772	1/60	6/60	C; 130 days	Unknown
Physical Medicine and Rehabilitation	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at Texas Medical Center Houston, Tex.	B Lim 60	IC	Lec	12	10/ 2/59	10/ 3/59	C; 2 days	Nil

PROCTOLOGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Proctology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14, Minn.	G Lim 30	IC	PD, Surg, Lec, Pan, O, AV	30	5/23/60	5/27/60	C; 5 days	65

Surgery PM 30—Office Proctology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	IC	Lec, O, AV	10	11/ 5/59 4/14/60	11/ 6/59	[illegible]	
Proctology, Colorectal Surgery, Operative Proctology on Cadaver	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV, TV, EPP	120	4/ 1/60 10/ 1/60	4/30/60	C; 21 days	150
Postgraduate Refresher Course in Proctology	University of Texas Postgraduate School of Medicine 213 W. Avenue G, Temple, Tex. course at Scott and White Memorial Hospital; Scott, Sherwood and Brindley Foundation, Temple, Tex.	G Lim 2	IC	PD, LC, BR, Surg, O	88	Arranged	2 weeks later	C; 12 days	25

PSYCHIATRY

(See also Pediatrics, Neurology and Psychiatry)

Dynamic Concepts of Medicine—A Two Day Symposium on Psychological Factors in Medical Practice	California Medical Association 2975 Wilshire Blvd., Los Angeles; course for Regional PG Institute West Coast County Societies, at Golden Bough Theater, Carmel	B	IC	Sem, Lec, Pan, O, AV	14	5/19/60	5/20/60	C; 2 days	25
Clinical Traineeship and Special Skills Course—Psychiatry	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
Psychiatry for General Practitioners	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 11	II	PD, Sem, Lec, Pan, O, AV	50	10/15/59	4/21/60	I; 25 sessions 2 hr. weekly, Thursdays	125
849—Psychiatric Problems in General Practice	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33 course at Los Angeles County Hospital	G Lim 100	II	Lec, Pan, O	22	10/ 8/59	12/17/59	I; 11 sessions 2 hr. weekly, Thursdays	50
850—Therapeutic Interviewing	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33 course at Los Angeles County Hospital	G Lim 15	II	PD, Lec, O	24	2/11/60	5/ 5/60	I; 12 sessions 2 hr. weekly, Thursdays	100
Psychiatry for General Practitioners—Recognition and Handling of Common Psychiatric Problems	Langley Porter Neuropsychiatric Institute Parnassus and First Aves., San Francisco	G Lim 24	II	PD, LC, Clin C, Sem, O, EPP	160	Spring/60		I; 32 sessions 5 hr. weekly, Wednesdays	25
Psychoanalytic Theory and Practice	San Francisco Psychoanalytic Institute 2235 Post St., San Francisco	S	II	Sem, Lec, O	Unknown	Unknown		I; 2, 2 hr. sessions a mo.	Unknown
13th Connecticut Postgraduate Seminar in Psychiatry and Neurology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S	II	Lec, O, AV	52	1/27/60	4/20/60	I; 4 hr. weekly	Nil
Social and Preventive Psychiatry	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D. C.	S (Military personnel only) Lim 25	IC	Clin C, Lec, Pan, O	21	1/25/60	1/27/60	C; 3 days	Nil
Office Management of Emotional Disorders	North Shore Hospital 225 Sheridan Rd., Winnetka, Ill.	G	II	Sem, Lec, O, AV	18	10/ 7/59	6/ 1/60	I; 9 sessions 2 hr. once a mo., Wednesdays	Nil
Psychiatry for General Practitioners	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	PD, Lec, Pan, O, AV	14	11/18/59	11/19/59	C; 2 days	20
Maintaining Emotional Health	The Menninger Foundation Topeka, Ks.	S	IC	PD, LC, Sem, Lec, O, EPP	40	3/ 7/60	3/11/60	C; 5 days	300
Clinical Traineeship in Psychiatry	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	BR, Clin C, Sem, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. nonresidents
MedicalSurgical Symposia—Part III. Psychiatry	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	O	PD, LC, Sem, Lec, Pan, O, AV	7	3/23/60	3/23/60	C; 1 day	20
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Unknown Lim 2	PT	PT	Full time	Arranged	2 weeks or more later		25 per week
Psychological Theories of Schizophrenia	Spring Grove School of Psychiatry Spring Grove State Hospital Catonsville 28, Md	S Lim 35	II	Sem, Lec, O	20	9/59	1/60	I; 10 sessions 2 hr. monthly, Wednesdays	25
Child Psychiatry	Spring Grove School of Psychiatry Spring Grove State Hospital Catonsville 28, Md.	S Lim 35	II	Sem, Lec, O	20	2/60	6/60	I; 10 sessions 2 hr. monthly, day not determined	25
Psychiatry	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 40	IC	PD, Clin C, Lec, O, AV	12	2/29/60	3/ 1/60	C; 2 days	25

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PSYCHIATRY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Office Psychotherapy for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	30	5/16/60	5/20/60	C; 5 days	65
Psychiatry in General Practice	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	PD, Clin C, Sem, Lec, TV	6	11/19/59 3/24/60	11/19/59	C; 1 day	10
Psychiatry and Psychotherapy	Department of Postgraduate Medical Education Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at East Orange, Veterans Administration Hospital, East Orange, N. J.	Unknown	II	Unknown		9/16/59	11/18/59	I; Wednesdays	Unknown
Psychiatric Problems in General Practice	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, Sem, Lec, Pan, O, AV	14	3/ 9/60	3/10/60	C; 2 days	30
Psychiatry for the General Practitioner	Marcy State Hospital Marcy, N.Y.	G Lim 40	II	PD, Sem	32	Unknown		I; 8 sessions 1 hr. weekly	Nil
Readings in Psychoanalysis. The Works of Karen Horney	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Sem, Lec, O	37½	9/14/59	4/25/60	I; 25 sessions 1½ hr. weekly, Mondays	85
Fundamentals of Psychoanalytic Technique	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Lec	30	9/14/59	2/ 1/60	I; 20 sessions 1½ hr. weekly, Mondays	100
Continuous Case Seminar	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem	18	9/15/59	12/ 1/59	I; 12 sessions 1½ hr. weekly, Tuesdays	60
Introduction to Psychoanalytic Technique	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem, Lec, O	15	9/15/59	11/17/59	I; 10 sessions 1½ hr. weekly, Tuesdays	40
Seminar on Child Therapy	American Institute for Psychoanalysis 220 W. 98th St., New York	G Lim 20	II	Sem, Lec	10½	9/25/59	11/ 6/59	I; 7 sessions 1½ hr. weekly, Fridays	28
Mothers and Fathers Today: Workshop	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 30	II	Sem	22½	9/28/59	1/11/60	I; 15 sessions 1½ hr. weekly, Mondays	45
Horney's Contributions to Psychoanalysis	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 30	II	Sem, Lec	22½	9/29/59	1/12/60	I; 15 sessions 1½ hr. weekly, Tuesdays	27
Clinical Conferences on Case Histories I	American Institute for Psychoanalysis 220 W. 98th St., New York	G Lim 30	II	Sem	15	11/20/59	2/ 5/60	I; 10 sessions 1½ hr. weekly, Fridays	40
Problems in Therapy—Postgraduate Course	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 15	II	Sem	15	1/15/60	3/18/60	I; 10 sessions 1½ hr. weekly, Fridays	50
Introductory Course on Dreams	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem, Lec, O	15	2/ 1/60	4/ 4/60	I; 10 sessions 1½ hr. weekly, Mondays	40
The Psychoanalytic Relationship	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 15	II	Sem, Lec	22½	2/ 2/60	5/17/60	I; 15 sessions 1½ hr. weekly, Tuesdays	75
Maturing: Frustration and Fulfillment	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Sem, Lec	22½	2/ 8/60	5/23/60	I; 15 sessions 1½ hr. weekly, Mondays	27
Present-Day Perspectives in Psychoanalysis	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Sem, Lec	22½	2/ 9/60	5/24/60	I; 15 sessions 1½ hr. weekly, Tuesdays	27
Clinical Conferences on Case Histories II	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem	15	2/16/60	4/19/60	I; 10 sessions 1½ hr. weekly, Tuesdays	40
Group Psychoanalysis	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Sem	15	2/19/60	4/22/60	I; 10 sessions 1½ hr. weekly, Fridays	40
Clinical Conferences	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem	15	2/22/60	4/25/60	I; 10 sessions 1½ hr. weekly, Mondays	50
Projective Tests in Psychoanalytic Practice	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G Lim 10	II	Lec	9	9/30/59	11/ 4/59	I; 6 sessions 1½ hr. weekly, Wednesdays	50
Psychosomatic Medicine	New York Medical College Flower and Fifth Ave. Hospitals	G Lim 10	II	Lec	12	10/ 6/59	11/24/59	I; 8 sessions 1½ hr. weekly,	65

Readings in Psychoanalytic Literature (First Half)	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G Lim 10	H	Lec	22½	10/ 6/59	1/12/60	I; 15 sessions 1½ hr. weekly, Tuesdays	50
Psychoanalysis in Groups	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	S Lim 15	H	Sem	15	10/ 9/59	12/11/59	I; 10 sessions 1½ hr. weekly, Fridays	10
Personality Structure and Psychoanalysis	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G Lim 15	H	Lec	15	10/13/59	12/15/59	I; 10 sessions 1½ hr. weekly, Tuesdays	50
Child Psychiatry	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G Lim 25	H	Lec	15	1/ 7/60	3/ 3/60	I; 10 sessions 1½ hr. weekly, Thursdays	10
703—The Development of Psychoanalytic Thinking	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Lec	24	9/28/59 2/ 8/60	1/18/60	I; 16 sessions 1½ hr. weekly, Mondays	60
Comprehensive Curriculum in Group Psychotherapy	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 15	H	LC, Sem	66	9/29/59 2/ 9/60	1/19/60	I; 4 hr. weekly, Tuesdays	160 for the yr.
718—Clinical Conference on Treatment or Planning	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Sem	24	9/29/59	1/19/60	I; 16 sessions 1½ hr. weekly, Tuesdays	60
731—Clinical Conferences	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Sem	7½	9/30/59 2/10/60	10/28/59	I; 5 sessions 1½ hr. weekly, Wednesdays	20
715—Introduction to Psychotherapy and Psychotherapeutic Techniques	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Lec, Clin C	24	9/30/59	1/20/60	I; 16 sessions 1½ hr. weekly, Wednesdays	60
706—Techniques of Dream Interpretation	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Sem	22½	10/ 1/59	1/21/60	I; 15 sessions 1½ hr. weekly, Thursdays	60
817n—Clinical Conference; Character Disorders	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Sem	15	2/ 8/60	4/25/60	I; 10 sessions 1½ hr. weekly, Mondays	40
818—The Borderline Patient	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Sem	22½	2/10/60	5/25/60	I; 15 sessions 1½ hr. weekly, Wednesdays	60
Dream Interpretation: Advanced Seminar	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	H	LC, Sem	15	3/16/60	5/25/60	I; 10 sessions 1½ hr. weekly, Wednesdays	60
Psychological Aspects of Medical Practice—Emotional Problems	Staunton Clinic, Department of Psychiatry University of Pittsburgh School of Medicine 3601 Fifth Ave., Pittsburgh 13, Pa.	G Lim 10 per section	H	Sem, O	26	9/16/59	12/16/59	I; 13 sessions 2 hr. weekly, Wednesdays or Thursdays	50
Clinical Psychiatry	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at Texas Medical Center Hospitals Houston, Tex.	G Lim 20	H	PD, LC, BR, Sem, Lec, EPP	144	9/ 1/59	6/60	I; 72 sessions 2 hr. twice weekly, Tuesdays, Thursdays	2 per hr.
Practical Psychiatry—Current Concepts	University of Washington School of Medicine Seattle, Wash.	B Lim 12	IC	PD, LC, BR, Clin C, Sem, Lec, O		Summer 1960		C; 5 days	Unknown
PUBLIC HEALTH AND PREVENTIVE MEDICINE									
Clinical Traineeship and Special Skills Course—Preventive Medicine and Public Health	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
Tropical Public Health—Causes, Treatment and Management of Diseases Found in Warm Climates	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G Planning to practice abroad	IC	Lab, Sem, Lec, O, AV	Unknown	1/ 1/60 Annually	5/30/60		65
Examination for Radioactive Contamination of Foods	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington, D. C.	G Military personnel only Lim 6	IC	Lec, O	320	9/28/59	11/20/59	C; 40 days	Nil
Clinical Traineeship in Public Health and Preventive Medicine	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Clin C, Lec, O, AV, EPP		Arranged		Arranged	50 mo. Kansas residents; 100 mo. non-residents
Extension Course in Public Health Qualifying for Grade II Local Health Officer in New York State	Albany Medical College New Scotland Ave., Albany, N. Y.	G	H	Sem, Lec, O	30	Any time	1 yr. later	I; 6 sessions Thursdays	25

Key will be found on page 1938.

PUBLIC HEALTH AND PREVENTIVE MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Occupational Medicine 207—Public Health Aspects of Radiation	Columbia University School of Public Health and Administrative Medicine 600 W. 168th St., New York 32	G	II	Lec, O, AV	18	3/28/60	5/27/60	I; 9 sessions	37

RADIOISOTOPES

(See also Basic Sciences, Radiology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
882a—Nuclear Medicine—Lectures in Physics and Clinical Application	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S	II	Lab, PD, LC, Lec, Pan, O	20	Unknown	Unknown	I; 20 sessions 1 hr. weekly, Fridays	50
882b—Nuclear Medicine—Practical Experience in Laboratory Techniques	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S Lim 8	II	Lab, PD, LC, Lec, Pan, O	24	Arranged		I; 8 sessions 3 hr. weekly	350
882c—Nuclear Medicine—Supervised Clinical Experience with Radioactive Isotopes	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S Lim 2	O	Lab, PD, LC, Lec, Pan, O, EPP	Unknown	Arranged		Arranged	175
Radiological Physics and Medical Use of Isotopes	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B Lim 20-25	II	PD, Sem, Lec	54	9/59	5/60	I; 36 sessions 1½ hr. weekly	10 per qtr.
Radiology 304—Radioactivity	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S Lim 10	II	Lab, O, EPP	36	3/10/60	5/26/60	I; 12 sessions 3 hr. weekly, Thursdays	150
The Clinical Uses of Radioisotopes	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 24	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	60	9/21/59 5/ 2/60	10/ 2/59	C; 10 days	200
Clinical Use of Radioactive Isotopes	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S	IC	Lab, IC, BR	40	Arranged		C; 5 days	50
Course in Medical uses of Radioactive Isotopes	Queens Hospital Center 82-68 164th St., Jamaica 32, N.Y.	S Lim 18	II	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	90	2/10/60	6/ 9/60	I; 18 sessions 5 hr. weekly, Tuesdays	250
Radiology PM 35—Use of Radioactive Iodine	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S Lim 2	II	Lab, PD, LC, Lec, O, AV	141	9/59 12/59 3/60	11/59	I; 48 sessions 3 hr. 4 times weekly, Mondays, Tuesdays, Thursdays, Friday	300
Radiology PM 41—Clinical Use of Radioactive Isotopes	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S Lim 22	II	Lab, PD, LC, Lec, AV	102	9/28/59	5/16/60	I; 34 sessions 3 hr. weekly, Mondays	300
Radiology PM 40—Clinical Use of Radioactive Isotopes	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S Lim 22	IC	Lab, PD, LC, Lec, O, AV	140	6/ 1/60	7/ 1/60	C; 20 days	300
Radioisotope Techniques in Diagnosis—Principles of Nuclear Physics. Instrumentation	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP		Arranged		4-6 weeks Arranged	150 for 4 weeks; 250 for 6 weeks
Radioisotopes for Therapeutic Uses—Handling, Dose Calculations, Therapeutic Uses	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave. and 106th St., New York	G	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP		Arranged		4-6 weeks Arranged	150 for 4 weeks; 250 for 6 weeks
654—Radioactive Isotopes	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 2	IC	Lab, PD, LC, BR, Clin C, Sem, EPP	150	Arranged	1 mo. later	C; 1 mo.	175
655—Radioactive Isotopes	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 1	II	Lab, PD, LC, BR, Clin C, Pan, EPP	102	10/ 7/59	5/25/60	I; 34 sessions 3 hr. weekly, Wednesdays	125
Radionuclide Protection (60R) in Medicine and Industry	Robert A. Taft Sanitary Engineering Center 4676 Columbia Parkway, Cincinnati 26	S Lim 28	IC	Lab, Lec, Pan, O, AV, EPP	35	10/19/59	10/23/59	C; 5 days	Nil
(1) Elements of Isotope Methodology, (2) Isotope Laboratory Practice (1) Basic Theory Nuclear Physics, (2) Applications	Hahnemann Medical College 235 N. 15th St., Philadelphia	S Lim 30	II	Lab, PD, Lec, Pan, O, EPP	39 lec 84 lab	10/59 3/60	12/59	I; 14 sessions 28 days	100 (no fee to residents, interns, etc.)
Course on Physical and Medical Aspects of Radioisotope Use	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	S and residents Lim 12	IC	Lab, PD, LC, Sem, Lec, Pan, EPP	160	1/ 4/60	1/29/60	C; 20 days	200
Clinical Application of Radioisotopes	School of Medicine, University of Puerto Rico	S	PT	Lab, PD, LC, BR, Clin C,		7/ 1/60	6/30/61		300

Clinical Application of Radioisotopes in Diagnosis and Therapy	School of Medicine, University of Puerto Rico San Juan 22, P. R.	S	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, EPP	180	7/ 1/60 8/ 1/60	9/30/60	C; 72 days	[illegible]
Basic Principles and the Application of Medical Isotopes	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at Engineering Building of The University of Texas, Austin, Tex.	S Lim 10	II	Unknown	90	9/21/59	3/10/60	I; 10 sessions weekly, 3 hr. Thursdays, 1 hr. Tuesdays	5

RADIOLOGY
(See also Anatomy)

Clinical Traineeship and Special Skills Course—Radiology	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
Diagnostic Radiology	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 200	IC	Lec, Pan, O, AV	35	3/60		C; 5 days	80
Radiology 302—Introduction to X-rays and Radioisotopes	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	II	Lec, O, AV	10	10/21/59	11/18/59	I; 5 sessions 2 hr. weekly, Wednesdays	25
Radiology 303—X-ray Physics	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	II	Lab, Dem, Lec, O, AV	20	12/ 3/59	2/18/60	I; 10 sessions 2 hr. weekly, Thursdays	40
Course I—Diagnostic Radiology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G	IC	Lab, PD, LC, Lec, O, AV, EPP	Unknown	Unknown		C; unknown	Unknown
Course II—Clinical Radiology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 6	IC	Lab, PD, LC, BR, Clin C, Sem, O	50	Arranged	2 wk. later	C; 12 days	70
Course III—X-Ray Therapy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, EPP	30 to 210	Arranged	1, 2, 4 or 8 wk. later	6 to 24 days	60 to 300
Radium Therapy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	Lab, PD, LC, BR, Surg, Lec, O	30	6/60	1 wk later	C; 5 days	100
Radiation Physics	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 60	II	Lec	26	1/11/60	5/ 9/60	I; 18 sessions 2 hr. weekly Mondays	50 physicians; 25 residents
Radiology of the Chest	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	S	IC	Clin C, Lec, Pan, O, AV	28	3/ 7/60	3/10/60	C; 4 days	75 General; 35 Residents
Radiological Physics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	II	Lec, O, AV	20	1/24/60	3/27/60	I; 10 sessions 2 hr. weekly, Sundays	30
Radiology and Radioactive Isotopes	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	Clin C, Lec, Pan, O, AV	21	2/ 8/60	2/10/60	C; 3 days	45
General Radiology 2	Harvard Medical School 25 Shattuck St., Boston; course at Peter Bent Brigham Hospital, Massachusetts General Hospital, Children's Hospital, Boston	S Lim 2	IC	Lab, PD, LC, Clin C, Sem	120-130 per mo.	Arranged		C; 26 days a mo.	150 per mo
Radiology, Diagnostic	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 10	IC	Lab, Lec, O, AV	18	4/ 4/60	4/ 6/60	C; 3 days	40
Radiology for Radiologists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S Lim 300	IC	Sem, Lec, Pan, O, AV	30	11/ 2/59	11/ 6/59	C; 5 days	100
Radiology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	15	4/11/60	4/13/60	C; 3 days	40
Cardiac Roentgenology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Elizabeth Hospital Elizabeth, N. J.	G Lim 10	II	PD, Clin C, Lec, O, AV	12	9/23/59	11/11/59	I; 8 sessions 1½ hr. weekly, Wednesdays	50
Course in Special Radiation Procedures in the Treatment of Cancer	Queens Hospital Center 82-68 164th St., Jamaica 32, N. Y.	S Lim 25	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, EPP	40	9/14/59	9/21/59	C; 5 days	150
Operative Radium Therapy	Queens Hospital Center 82-68 164th St., Jamaica 32, N. Y.	S Lim 7	II	PD, LC, BR, Clin C, Surg, Lec, O	32	First Saturday in Nov.	End of Dec. 1959	I; 8 sessions 4 hr. weekly, Saturdays	100
Radiology PM 51—Radiotherapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	IC	Lab, LC, Lec, O, EPP	6 or 12 mo.	Arranged	6 or 12 mo. later	Arranged	300 for 6 mo.; 600 for 12 mo.

Key will be found on page 1938.

RADIOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
gy PM 31—Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	B	IC	Lec, AV, O	10½	9/28/59	10/ 6/59	C; 7 days	50
Radiology PM 80—Roentgenographic Interpretation of Diseases of the Bones and Joints	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Hospital for Joint Diseases New York 35	S	II	Lec, O, AV	24	9/30/59	12/16/59	I; 12 sessions 2 hr. weekly, Wednesdays	150
Radiology PM 36—Differential Diagnosis in Gastrointestinal Radiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G Lim 3	II	PD, LC, Sem	10	10/13/59 3/29/60	12/15/59	I; 10 sessions 1 hr. weekly, Tuesdays	50
Radiology PM 34—Chest, Differential Diagnosis in Radiology of the Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G Lim 3	II	PD, LC, Sem	15	10/19/59 3/14/60	12/21/59	I; 10 sessions 1½ hr. weekly, Mondays	50
Radiology PM 1—Radiological Physics	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	II	Lec, O, AV	36	1/ 5/60	5/ 5/60	I; 36 sessions 1 hr. twice weekly, Tuesdays, Thursdays	50
Radiology PM 32—Roentgen Diagnosis of Lesions of the Gastrointestinal Tract, Gall Bladder, and Pancreas	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	IC	Lec, O, AV	10½	3/14/60	3/22/60	C; 7 days	50
Radiology PM 2—Neuro-Radiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	IC	PD, Lec, Pan, O, AV	37½	4/11/60	4/15/60	C; 5 days	100
Radiology PM 33—Radium Therapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	II	Lec, O, AV	12	5/17/60	6/21/60	I; *6 sessions* 2 hr. weekly, Tuesdays	50
Radiology PM 52—Megavoltage Therapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	II	Lec, O, AV	12	5/19/60	6/23/60	I; 6 sessions 2 hr. weekly, Thursdays	[illegible]
Roentgen Diagnosis in Gastroenterology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Beth-El Hospital, Brooklyn, N. Y.	G Lim 20	II	Lec, O	8	10/59	12/59	I; 8 sessions 1 hr. weekly, Tuesdays	20
Diagnostic Roentgenology in Desired Field	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP		Arranged		4-6 weeks arranged	150 for 4 wks.; 250 for 6 wks.
Radiation Physics and Protection—Principles of Physics, X-ray Production, Measurement	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G	PT	Lab, PD, LC, Clin C, Sem, Lec, Pan, O, EPP		Arranged		4-6 weeks arranged	150 for 4 wks.; 250 for 6 wks.
Radium and Roentgen Therapy—Individualized	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G	PT	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O		Arranged		4-6 weeks arranged	150 for 4 wks.; 250 for 6 wks.
Practical Roentgenological Interpretation	*New York Polyclinic Hospital* 315 W. 50th St., New York 19	G Lim 12	IC	PD, LC, Lec	180	4/ 1/60 10/ 1/60	6/30/60	C; 72 days	300
653—Clinical Radiation Therapy	New York University Post-Graduate Medical Schoc	G Lim 2	II	PD, LC, BR, Clin C, Sem, Lec, O	54	9/20/59	1/27/60	I; 18 sessions 3 hr. weekly, Wednesdays	100
		G [illegible] 50	II	Lec	60	9/23/59	1/27/60	I; 30 sessions 2 hr. weekly, Wednesdays	125
			IC	Lab, Lec, AV	70	10/12/59	10/23/59	C; 10 days	100
		[illegible] non- [illegible]icians Lim 10	IC	Lab, Lec, AV	70	10/26/59	11/ 6/59	C; 10 days	100

652—Radiobiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	Sem, Lec	34	2/ 3/60	5/25/60	I: 17 sessions 2 hr. weekly, Wednesdays	Unknown
1813—Radiation Hygiene Measurements	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 16	IC	Lab, Lec, AV	140	4/18/60	5/13/60	C: 20 days	200
General Roentgenology	Goldwater Memorial Hospital Welfare Island, New York	B Lim 3	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP		Arranged	1 yr. later	5½ days weekly	Unknown
X-Ray Protection	Chief, Radiological Health Training Activities; Division of Radiological Health, U. S. Public Health Service; Robert A. Taft Sanitary Engineering Center 4676 Columbia Pkwy., Cincinnati 26	S Lim 30	IC	Lab, Lec, O, AV, EPP	30	10/26/59	10/30/59	C: 5 days	Nil
Medical Aspects of *Radiological* Health (50R)—Biological Effects of Radiation, Safe Practices with Radionuclides and X-rays.	Robert A. Taft Sanitary Engineering Center 4676 Columbia Pkwy., Cincinnati 26	G Lim 28	IC	Lab, Lec, Pan, O, AV, EPP	70	11/30/59	12/11/59	C: 10 days	Nil
Advanced Radiotherapy—Instruction and Demonstration of Low, Medium and Supervoltage Radiotherapy, Curietherapy and Their Application to Cancer	University of Puerto Rico, Puerto Rico Nuclear Center, Mayaguez, P. R.: course at Dr. I. Gonzalez Martinez Oncologic Hospital, San Juan, P. R.	S		PD, LC, BR, Clin C, Sem, Lec, O		Arranged	At least 30 days later		25
Practical Course in Radiological Physics	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex ; course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	S and residents Lim 6	IC	Lab, Sem, Lec, EPP	160	2/ 1/60	3/25/60	C: 10 days	200

SURGERY

(See also Anatomy, Cardiovascular Disease, Peripheral Vascular Disease)

Clinical Traineeship and Special Skills Course—Surgery	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
A Series of Postgraduate Surgical Clinics and Symposia	U.S. Veterans Administration Hospital (Fort Miley) 42nd Ave. and Clement St., San Francisco	G Lim 300	II	Lab, PD, LC, Sem, Lec, Pan, O	12	9/22/59	11/ 3/59	I: 6 sessions 2 hr. weekly, Tuesdays	15 AAGP members; 20 non-members; no fee interns and residents
Surgical and Orthopedic Aspects of Trauma	*Department* of the Army Office of the Surgeon General Education and Training Division Washington 25, D.C.; course at Brooke Army Hospital, Brooke Army Medical Center, Fort Sam Houston, Tex.	B Lim 100	IC	PD, BR, Clin C, Sem, Lec, Pan, O	35	3/14/60	3/18/60	C: 5 days	Nil
Surgery in Acute Trauma	Department of the Army Office of the Surgeon General Education and Training Division *Washington* 25, D.C.; course at Fitzsimons Army Hospital, Denver	G Lim 100	IC	Sem, Lec, Pan, O	24	4/ 4/60	4/ 6/60	C: 3 days	Nil
Symposium on Current Surgical Practices	*Department* of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D.C.; course at Walter Reed Army *Institute* of Research, Washington 12, D.C.	S (Military personnel only) *Lim* 75	IC	PD, Clin C, Sem, Lec, O TV	20	4/18/60	4/20/60	C: 3 days	Nil
Seminar in Surgery—Recent Advances	University of Florida College of Medicine Gainesville, Fla.	B	IC	PD, Clin C, Sem, Lec, Pan, O	15	1/14/60	1/16/60	C: 2½ days	25
Trauma	Emory University School of Medicine 69 Butler St., S.E., Atlanta 3, Ga.	S	IC	Unknown	40	10/26/59	10/30/59	C: 5 days	Unknown
Course I—Surgical Technic in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Surg, Lec, O, AV, EPP	90	9/21/59 10/19/59 11/30/59 Once each mo. during 1960	10/ 2/59	C: 11 days	250
Surgery of Colon and Rectum	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 18	IC	Lab, PD, LC, BR, Surg, Lec, O, AV	35	9/21/59 10/26/59 11/30/59 2/22/60 4/ 4/60 5/ 2/60 6/ 6/60	9/25/59	C: 5 days	125
General Surgery—Board Review Part I	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 40	IC	Lab, PD, LC, BR, Surg, Lec, O, EPP	110	10/ 5/59	10/17/59	C: 12 days	300

Key will be found on page 1938.

RADIOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Radiology PM 31—Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	B	IC	Lec, AV, O	10½	9/28/59	10/ 6/59	C; 7 days	50
Radiology PM 80—Roentgenographic Interpretation of Diseases of the Bones and Joints	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Hospital for Joint Diseases New York 35	S	II	Lec, O, AV	24	9/30/59	12/10/59	I; 12 sessions 2 hr. weekly, Wednesdays	150
Radiology PM 30—Differential Diagnosis in Gastrointestinal Radiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G Lim 3	II	PD, LC, Sem	10	10/13/59 3/29/60	12/15/59	I; 10 sessions 1 hr. weekly, Tuesdays	50
Radiology PM 34—Chest, Differential Diagnosis in Radiology of the Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G Lim 3	II	PD, LC, Sem	15	10/19/59 3/14/60	12/21/59	I; 10 sessions 1½ hr. weekly, Mondays	50
Radiology PM 1—Radiological Physics	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	II	Lec, O, AV	36	1/ 5/60	5/ 5/60	I; 36 sessions 1 hr. twice weekly, Tuesdays, Thursdays	50
Radiology PM 32—Roentgen Diagnosis of Lesions of the Gastrointestinal Tract, Gall Bladder, and Pancreas	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	G	IC	Lec, O, AV	10½	3/14/60	3/22/60	C; 7 days	50
Radiology PM 2—Neuro-Radiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	IC	PD, Lec, Pan, O, AV	37½	4/11/60	4/15/60	C; 5 days	100
Radiology PM 33—Radium Therapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	II	Lec, O, AV	12	5/17/60	6/21/60	I; 6 sessions 2 hr. weekly, Tuesdays	50
Radiology PM 52—Megavoltage Therapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	II	Lec, O, AV	12	5/19/60	6/23/60	I; 6 sessions 2 hr. weekly, Thursdays	[illegible]
Roentgen Diagnosis in Gastroenterology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Beth-El Hospital, Brooklyn, N. Y.	G Lim 20	II	Lec, O	8	10/59	12/59	I; 8 sessions 1 hr. weekly, Tuesdays	20
Diagnostic Roentgenology in Desired Field	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP		Arranged		4-6 weeks arranged	150 for 4 wks.; 250 for 6 wks.
Radiation Physics and Protection—Principles of Physics, X-ray Production, Measurement	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G	PT	Lab, PD, LC, Clin C, Sem, Lec, Pan, O, EPP		Arranged		4-6 weeks arranged	150 for 4 wks.; 250 for 6 wks.
Radium and Roentgen Therapy—Individualized	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York	G	PT	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O		Arranged		4-6 weeks arranged	150 for 4 wks.; 250 for 6 wks.
Practical Roentgenological Interpretation	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	PD, LC, Lec	180	4/ 1/60 10/ 1/60	6/30/60	C; 72 days	300
653—Clinical Radiation Therapy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 2	II	PD, LC, BR, Clin C, Sem, Lec, O	54	9/20/59	1/27/60	I; 18 sessions 3 hr. weekly, Wednesdays	100
651—Diagnostic Radiology for General Practitioners	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 50	II	Lec	60	9/23/59	4/27/60	I; 30 sessions 2 hr. weekly, Wednesdays	125
1812—Introduction to Radiological Health	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-physicians Lim 35	IC	Lab, Lec, AV	70	10/12/59	10/23/59	C; 10 days	100
1812-L—Radiological Health Laboratory	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-physicians Lim 10	IC	Lab, Lec, AV	70	10/26/59	11/ 6/59	C; 10 days	100

652—Radiobiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	Sem, *Lec*	34	2/ 3/60	5/25/60	I: 17 sessions 2 hr. weekly, Wednesdays	Unknown
4813—Radiation Hygiene *Measurements*	New York University *Post-Graduate* Medical School 550 First Ave., New York 16	G Lim 16	IC	Lab, Lec, AV	140	4/18/60	5/13/60	C; 20 days	200
General Roentgenology	Goldwater Memorial Hospital Welfare Island, New York	B Lim 3	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP		Arranged	1 yr. later	5½ days weekly	Unknown
X-Ray Protection	*Chief, Radiological Health Training Activities;* Division of Radiological Health, U. S. Public Health Service; Robert A. Taft Sanitary Engineering Center 4676 Columbia Pkwy., Cincinnati 26	S Lim 30	IC	Lab, Lec, O, AV, EPP	30	10/26/59	10/30/59	C; 5 days	Nil
Medical Aspects of *Radiological* Health (50R)—Biological Effects of Radiation, Safe *Practices* with Radionuclides and X-rays.	Robert A. Taft Sanitary Engineering Center 4676 Columbia Pkwy., Cincinnati 26	G Lim 28	IC	Lab, Lec, Pan, O, AV, EPP	70	11/30/59	12/11/59	C; 10 days	Nil
Advanced Radiotherapy—Instruction *and* Demonstration of Low, Medium and Supervoltage Radiotherapy, Curietherapy and Their Application to Cancer	*University of Puerto Rico,* Puerto Rico Nuclear Center, Mayaguez, P. R.: course at *Dr. I. Gonzalez Martinez* Oncologic Hospital, San Juan, P. R.	S		PD, LC, BR, Clin C, Sem, Lec, O		Arranged	At least 30 days later		25
Practical Course in *Radiological* Physics	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Tex.	S *and residents* Lim 6	IC	Lab, Sem, Lec, EPP	160	2/ 1/60	3/25/60	C; 40 days	200

SURGERY

(See also Anatomy, Cardiovascular Disease, Peripheral Vascular Disease)

Clinical Traineeship and Special *Skills Course—Surgery*	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G	PT	PT	Arranged	Arranged	2 weeks later	Full time	Unknown
A Series of Postgraduate Surgical Clinics and Symposia	U.S. Veterans Administration Hospital (Fort Miley) 42nd Ave. and Clement St., San Francisco	G Lim 300	II	Lab, PD, LC, Sem, Lec, Pan, O	12	9/22/59	11/ 3/59	I: 6 sessions 2 hr. weekly, Tuesdays	15 AAGP members; 20 non-members; no fee interns and residents
Surgical and Orthopedic Aspects of Trauma	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D.C.; course at Brooke Army Hospital, Brooke Army Medical Center, Fort Sam Houston, Tex.	B Lim 100	IC	PD, BR, Clin C, Sem, Lec, Pan, O	35	3/14/60	3/18/60	C; 5 days	Nil
Surgery in Acute Trauma	Department of the Army Office of the Surgeon General Education and Training *Division* Washington 25, D.C.; course at Fitzsimons Army Hospital, Denver	G Lim 100	IC	Sem, Lec, Pan, O	24	4/ 4/60	4/ 6/60	C; 3 days	Nil
Symposium on Current Surgical Practices	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D.C.; course at Walter Reed Army Institute of Research, Washington 12, D.C.	S (Military personnel only) Lim 75	IC	PD, Clin C, Sem, Lec, O TV	20	4/18/60	4/20/60	C; 3 days	Nil
Seminar in Surgery—Recent Advances	University of Florida College of Medicine Gainesville, Fla.	B	IC	PD, Clin C, Sem, Lec, Pan, O	15	1/14/60	1/16/60	C; 2½ days	25
Trauma	Emory University School of *Medicine* 69 Butler St., S.E., Atlanta 3, Ga.	S	IC	Unknown	40	10/26/59	10/30/59	C; 5 days	Unknown
Course I—Surgical Technic in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Surg, Lec, O, AV, EPP	90	9/21/59 10/19/59 11/30/59 Once each mo. during 1960	10/ 2/59	C; 11 days	250
Surgery of Colon and Rectum	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 18	IC	Lab, PD, LC, BR, Surg, Lec, O, AV	35	9/21/59 10/26/59 11/30/59 2/22/60 4/ 4/60 5/ 2/60 6/ 6/60	9/25/59	C; 5 days	125
General Surgery—Board Review Part I	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 10	IC	Lab, PD, LC, BR, Surg, Lec, O, EPP	110	10/ 5/59	10/17/59	C; 12 days	300

Key will be found on page 1938.

SURGERY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Thoracic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 18	IC	Lab, PD, LC, BR, Surg, Lec, O	30	10/19/59 6/20/60	10/23/59	C; 5 days	125
Surgery of the Hand	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 16	IC	Lab, PD, LC, BR, Surg, Lec, O, AV, EPP	35	10/26/59 Spring/60	10/30/59	C; 5 days	150
One Week Course in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	PD, LC, BR, Surg, Lec, O	25	10/26/59 2/60 5/60 6/60	10/30/59	C; 5 days	150
Annual Postgraduate Course of the United States Section of the International College of Surgeons	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 50	IC	Lab, PD, LC, Surg, Lec, O, AV, EPP	78	11/ 2/59 4/11/60 8/ 1/60	11/13/59	C; 11 days	175
Basic Principles in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 50	IC	Lab, PD, LC, BR, Surg, Lec, O, AV, EPP	78	11/ 2/59 4/11/60 8/ 1/60	11/13/59	C; 11 days	175
Gallbladder Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	PD, LC, BR, Surg, Lec, O, AV	10	11/ 3/59 Offered 3 times during 1960	11/ 5/59	C; 3 days	80
Surgery of Hernia	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O	13	11/ 5/59 Offered 3 times during 1960	11/ 7/59	C; 3 days	80
Head, Neck and Plastic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 24	IC	Lab, PD, LC, BR, Sem, Surg, Lec, O, EPP	40	11/16/59 In 1960 dates not known	11/20/59	C; 5 days	150
Blood Vessel Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 40	IC	Lab, PD, LC, BR, Surg, Lec, O, EPP	35	11/30/59 Spring and Summer, 1960	12/ 4/59	C; 5 days	175
Pediatric Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	Lab, PD, LC, BR, Surg, Lec, O	35	12/ 7/59 Spring/60	12/11/59	C; 5 days	150
Two-Week Course in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 20	IC	Lab, PD, LC, BR, Surg, Lec, O, AY	70	12/ 7/59 5/ 2/60	12/18/59	C; 11 days	250
Breast and Thyroid Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 18	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	34	5/ 2/60	5/ 7/60	C; 6 days	150
General Surgery—Board Review Part II	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 40	IC	Lab, PD, LC, BR, Surg, Lec, O, EPP	110	5/ 9/60	5/21/60	C; 12 days	300
Surgery	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	3/16/60	3/16/60	C; 1 day	10
Surgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Clin C, Lec, Pan, O, AV, TV	28	5/23/60	5/26/60	C; 4 days	60
Clinical Traineeship	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	Unknown Lim 2	PT	PT	full time	Arranged	1 week or more later		25 per week
General Surgery I	Harvard Medical School 25 Shattuck St., Boston; course at Massachusetts General Hospital, Boston	G Lim 25	IC	PD, LC, BR, Clin C, Lec	110	10/ 5/59 6/ 6/60	10/23/59	C; 15 days	250
Clinical Exercises for Practitioners	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	II	PD, Clin C, Lec, O, AV	60	10/ 7/59	3/ 2/60	I; weekly Wednesdays	65
Surgery for Surgeons	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Surg, Lec, Pan, O, AV	15	1/21/60	1/23/60	C; 3 days	40
Emergency Surgery for Surgeons	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	4/ 7/60	4/ 9/60	C; 3 days	40
Surgery Traineeship	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	PT	PD, LC, BR, Clin C, Sem, O, Pan, EPP	40	11/ 9/59	11/14/59	C; 5½ days	75
Plastic Surgery of the Face	Newark Eye and Ear Infirmary 77 Central Ave., Newark, N. J.	S Lim 16	II	PD, LC, Surg, Lec	8	2/ 4/60	2/25/60	I; 4 sessions 2 hr. weekly, Thursdays	Nil
Newer Concepts in General Surgery	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at St. Barnabas Medical Center, Newark, N. J.	G Lim 40	II	PD, Clin C, Lec, O, AV	15	10/ 7/59	12/16/59	I; 10 sessions 1½ hr. weekly, Wednesdays	50

Experimental Gastro-Intestinal Surgery on Animals	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 15	II	Lab, Surg, Lec, O, AV, EPP	18	10/17/59	11/21/59	I; 6 sessions 3 hr. weekly, Saturdays	150
Plastic Procedures in General Surgery	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at St. Barnabas Medical Center, Newark, N. J.	G Lim 35	II	PD, LC, Clin C, Lec, O, AV	6	1/ 7/60	2/11/60	I; 6 sessions 1 hr. weekly, Thursdays	50
Traumatic Surgery	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 45	II	PD, Clin C, Lec, O,	15	1/13/60	3/16/60	I; 10 sessions 1½ hr. weekly, Wednesdays	50
One Day Seminar in General Surgery	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark 2, N. J.; course at St. Francis Hospital, Trenton, N. J.	G Lim 40	IC	Unknown	8	1/14/60	1/14/60	C; 1 day	25
Experimental Vascular Surgery on Animals	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 15	II	Lab, Lec, O, AV, EPP	33	1/16/60	3/19/60	I; 11 sessions 3 hr. weekly, Saturdays	225
Clinical Surgery	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at St. Mary's Hospital, Passaic, N. J.	B Lim 45	II	PD, Clin C, Lec, O, AV	18	2/18/60	5/ 5/60	I; 12 sessions 1½ hr. weekly, Thursdays	50
Experimental Genitourinary Surgery on Animals	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 15	II	Lab, Surg, Lec, O, AV	9	4/ 2/60	4/16/60	I; 3 sessions 3 hr. weekly, Saturdays	60
Experimental Pelvic Surgery on Animals	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 15	II	Lab, Surg, Lec, O, AV	9	4/23/60	5/ 7/60	I; 3 sessions 3 hr. weekly, Saturdays	60
Special Teaching Day in Surgery	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	Sem, Lec, Pan, O, AV	5	1/ 7/60	1/ 7/60	C; 1 day	12
Office Surgery	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at St. Johns Episcopal Hospital, Brooklyn, N.Y.	G Lim 20	II	PD, BR, Lec	12	10/59	12/59	I; 8 sessions 1½ hr. weekly, Tuesdays	20
Surgery PM 31—Minor Surgery for General Practitioners	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G Lim 10	IC	PD, LC, Clin C, Sem, Surg, Lec, O	21¾	11/30/59	12/ 2/59	C; 3 days	75
Advances in Surgical Technics, Diagnosis and Therapy	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 24	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	160	4/ 1/60 10/ 1/60	4/30/60	C; 24 days	350
661—Modern Concepts of Etiology, Pathologic Physiology and Therapy of Diseases with Surgical Implications	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 500	II	PD, Clin C, Lec, Pan, O, AV	111	9/10/59	6/15/60	I; 37 sessions 3 hr. weekly, Thursdays	300
551—The Intervertebral Disc	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 6	IC	PD, BR, Clin C, Surg, AV	14	10/ 8/59	10/ 9/59	C; 2 days	50
662—Surgery of the Hand	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, Clin C, Sem, Surg, Lec, AV	12	10/12/59 3/14/60	10/17/59	C; 6 days	115
663—Review of Surgery of the Stomach, Duodenum and Small Intestine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, LC, Lec, AV	35	10/26/59 3/ 7/60	10/30/59	C; 5 days	125
664—Review of the Surgery of the Biliary Tract and Pancreas	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, LC, Lec, AV	35	11/ 2/59 3/14/60	11/ 6/59	C; 5 days	125

Key will be found on page 1938.

SURGERY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
665—Review of Surgery of the Colon and Rectum	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, LC, Lec, AV	35	11/ 9/59 3/21/60	11/13/59	C; 5 days	125
666—Review of Surgery of the Head and Neck, Including Thyroid	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, LC, Lec, AV	35	11/16/59	11/20/59	C; 5 days	125
667—Review of Abdominal Surgical Diseases in Children	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, LC, Lec, AV	21	11/23/59 4/ 6/60	11/25/59	C; 3 days	60
552—Diagnosis and Treatment of Peripheral Nerve Injuries	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 8	IC	Lab, PD, Surg, Lec, EPP	11	1/ 7/60	1/ 8/60	C; 2 days	50
668—Basic Problems in Cancer Therapy (For Surgeons)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	Lab, PD, Clin C, Sem, Lec, Pan, O, AV	88	1/18/60	1/30/60	C; 12 days	225
Office Surgery	Albert Einstein Medical Center Southern Division Fifth and Reed Sts., Philadelphia 47	G Lim 20	II	PD, LC, Surg, Lec, O, AV	36	11/ 5/59	2/11/60	I; 12 sessions 3 hr. weekly, Thursdays	75
Surgery	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Robert B. Green Memorial Hospital, San Antonio, Tex.	G Lim 50	IC	Lec, AV	6	5/60	5/60	C; 1 day	10
Orthopedics and Traumatic Surgery	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Turner Home, El Paso, Tex.	G Lim 60	IC	Lec, O, AV	7	9/20/59	9/20/59	C; 1 day	10
Annual Symposium of Washington State Heart Association—Cardiac Surgery—Pulmonary Circulation	*University of Washington School of Medicine, Seattle 5*	*G* Lim 500	IC	Sem, Lec, *O*	9	10/16/59	10/17/59	C; 1½ days	*Unknown*

UROLOGY

(See also Anatomy, Basic Sciences, Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
James C. Kimbrough Urological Seminar	Department of the Army Office of the Surgeon General Education and Training Division Washington 25, D. C.; course at Brooke Army Hospital, Brooke Army Medical Center, Ft. Sam Houston, Tex.	S Lim 75	IC	Clin C, Sem, Lec, Pan, O, AV	24	11/ 2/59	11/ 4/59	C; 3 days	Nil
Urology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	80	10/26/59 3/28/60	11/ 7/59	C; 12 days	250
Office Urology	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	7	12/10/59	12/10/59	C; 1 day	10
Seminar on Genitourinary Problems	Department of Postgraduate Medical Education Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 40	IC	Sem, Lec, Pan, O, AV	9	1/13/60	1/27/60	I; 3 sessions 3 hr. weekly, Saturdays	Unknown
Urology Refresher Course for the General Practitioner	New York Medical College Flower and Fifth Ave. Hospitals Fifth Ave., and 106th St., New York; course at Metropolitan Hospital, New York	G Lim 15	IC	PD, LC, BR, Clin C	18	3/21/60	3/23/60	C; 3 days	30
Instrumental and Operative Urology	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Lec, Pan, O, AV, EPP	64	4/ 1/60 10/ 1/60	4/30/60	C; 21 days	250
671—Refresher Course in Basic Urology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	IC	Lab, Lec, O, EPP	35	1/11/60	1/15/60	C; 5 days	75
671-A. Advanced Course in Urology (For Specialists)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 16	IC	Lab, PD, BR, Clin C, Sem, Lec, O, EPP	42	5/ 2/60	5/ 7/60	C; 6 days	200
Recent Advances in Urology	Frank E. Bunts Educational Institute 2020 E. 93rd St., Cleveland, Ohio	B Lim 125	IC	LC, Sem, Lec, Pan, O, AV	12	9/16/59	9/17/59	C; 2 days	30

Key will be found on page 1938.

GEOGRAPHIC CROSS-REFERENCE

STATE	CATEGORY
ALABAMA	
Fairfield	Anesthesiology General Medicine
Montgomery	Clinical Pathology
Tuskegee	General Medicine
CALIFORNIA	
Carmel	Psychiatry
Long Beach	General Medicine
Los Angeles	Anesthesiology Cardiovascular Disease Chest Disease Clinical Pathology Dermatology Electrocardiography Endocrinology Gastroenterology General Medicine Hematology Internal Medicine Neurology Occupational Medicine Otolaryngology Pediatrics Physical Medicine and Rehabilitation Psychiatry Public Health and Preventive Medicine Radioisotopes Radiology Surgery
Martinez	General Medicine
Oakland	Endocrinology General Medicine
Palm Springs	General Medicine
San Diego	Anatomy Cardiovascular Disease General Medicine
San Francisco	Anatomy Basic Sciences Cardiovascular Disease Dermatology Electrocardiography Endocrinology Ephebology General Medicine Internal Medicine Obstetrics Ophthalmology Orthopedic Surgery Otolaryngology Pediatrics Physical Medicine Psychiatry Radiology Surgery
Santa Ana	Cardiovascular Disease
Santa Barbara	Cardiovascular Disease
Santa Monica	General Medicine
Santa Rosa	Cardiovascular Disease
Tahoe City	General Medicine
COLORADO	
Colorado Springs	General Medicine
Denver	Anatomy Cardiovascular Disease Chest Disease Dermatology Electrocardiography General Medicine Hematology Obstetrics and Gynecology Occupational Medicine Ophthalmology Physical Medicine and Rehabilitation Radioisotopes Surgery
Estes Park	Basic Sciences Pediatrics
CONNECTICUT	
New Haven	Anatomy Basic Sciences Electrocardiography General Medicine Neurology Pathology Pediatrics Psychiatry Radioisotopes Radiology
WASHINGTON, D.C.	Allergy General Medicine Internal Medicine Obstetrics and Gynecology Ophthalmology Pathology Pediatrics
WASHINGTON, D. C. (continued)	Psychiatry Public Health and Preventive Medicine Surgery
FLORIDA	
Gainesville	Neurology Obstetrics and Gynecology Pediatrics Surgery
Miami	Pathology
Miami Beach	Allergy Electrocardiography General Medicine Internal Medicine
GEORGIA	
Atlanta	Electrocardiography Internal Medicine Ophthalmology Surgery
Augusta	Fractures Internal Medicine
Warm Springs	Physical Medicine and Rehabilitation
ILLINOIS	
Belleville	General Medicine
Centralia	General Medicine
Chicago	All categories except: Anatomy Cardiovascular Disease Clinical Pathology Ephebology Malignant Disease Neurology Neurology and Psychiatry Obstetrics and Gynecology Occupational Medicine Ophthalmology and Otolaryngology Physical Medicine Proctology Public Health and Preventive Medicine
Effingham	General Medicine
Geneva	General Medicine
Herrin	General Medicine
Moline	General Medicine
Mt. Carmel	General Medicine
Ottawa	General Medicine
Rockford	General Medicine
Waukegan	General Medicine
INDIANA	
Indianapolis	Anesthesiology Cardiovascular Disease Electrocardiography Endocrinology Internal Medicine Malignant Disease Obstetrics and Gynecology Orthopedic Surgery Otolaryngology Pediatrics Psychiatry Radiology Surgery Urology
IOWA	
Iowa City	Cardiovascular Disease
KANSAS	
Chanute	General Medicine
Colby	General Medicine
Concordia	General Medicine
Dodge City	General Medicine
Emporia	General Medicine
Hutchinson	General Medicine
Kansas City	All categories except: Allergy Anatomy Clinical Pathology Dermatology Endoscopy Ephebology Malignant Disease Neurology and Psychiatry Obstetrics Obstetrics and Gynecology Peripheral Vascular Disease Proctology Radioisotopes Urology
Kays	General Medicine

STATE	CATEGORY
KANSAS (continued)	
Manhattan	General Medicine
Topeka	Psychiatry
Winfield	General Medicine
KENTUCKY	
Lexington	General Medicine
Louisville	General Medicine Pediatrics
LOUISIANA	
New Orleans	Anesthesiology Fractures Gastroenterology Internal Medicine Obstetrics and Gynecology Orthopedic Surgery Otolaryngology Pediatrics Psychiatry Surgery
Shreveport	General Medicine
MAINE	
Portland	Anesthesiology Electrocardiography
Waterville	Occupational Medicine Ophthalmology
MARYLAND	
Baltimore	Anatomy Basic Science Internal Medicine Occupational Medicine Pathology
Catonsville	Psychiatry
Edgewood	Occupational Medicine
MASSACHUSETTS	
Boston	Allergy Anatomy Basic Sciences Cardiovascular Disease Dermatology Electrocardiography Ephebology General Medicine Gynecology Hematology Internal Medicine Neurology Obstetrics Ophthalmology Orthopedic Surgery Pathology Pediatrics Radiology Surgery
Brookline	Gynecology
Worcester	General Medicine
Westfield	Malignant Disease
MICHIGAN	
Alpena	General Medicine
Ann Arbor	Allergy Anatomy Basic Sciences Cardiovascular Disease Dermatology Electrocardiography Endocrinology Gastroenterology General Medicine Internal Medicine Neurology Obstetrics and Gynecology Ophthalmology Otolaryngology Pathology Pediatrics Psychiatry Radioisotopes Radiology Surgery
Battle Creek	General Medicine
Bay City	General Medicine
Calumet	General Medicine
Cadillac	General Medicine
Detroit	Internal Medicine
Escanaba	General Medicine
Highland Park	Electrocardiography Internal Medicine
Iron Mountain	General Medicine
Ironwood	General Medicine
Jackson	General Medicine
Lansing	General Medicine
Marquette	General Medicine
Menominee	General Medicine
Muskegon	General Medicine

STATE	CATEGORY
MICHIGAN (continued)	
Niles	General Medicine
Roscommon	General Medicine
Sault St. Marie	General Medicine
MINNESOTA	
Leamington	Physical Medicine and Rehabilitation
Minneapolis	Cardiovascular Disease Dermatology Electrocardiography Endocrinology Fractures General Medicine Gynecology Internal Medicine Neurology Obstetrics Ophthalmology Otolaryngology Pediatrics Physical Medicine Psychiatry Radiology Surgery
Rochester	Ophthalmology Otolaryngology Pediatrics
MISSISSIPPI	
Greenwood	General Medicine
Gulfport	General Medicine
Hattiesburg	General Medicine
Jackson	Cardiovascular Disease General Medicine Malignant Disease
Meridian	General Medicine
Tupelo	General Medicine
MISSOURI	
Columbia	Anesthesiology Cardiovascular Disease
St. Joseph	General Medicine
St. Louis	Allergy Cardiovascular Disease
NEBRASKA	
Omaha	Electrocardiography General Medicine Internal Medicine Obstetrics and Gynecology Pediatrics Psychiatry Surgery
NEW JERSEY	
East Orange	Psychiatry
Elizabeth	Chest Disease Internal Medicine Radiology
Jersey City	Anatomy Obstetrics
Long Branch	General Medicine
Montclair	Neurology
Neptune	Cardiovascular Disease
Newark	Anesthesiology Basic Sciences Cardiovascular Disease Electrocardiography Gynecology Internal Medicine Obstetrics and Gynecology Ophthalmology Pediatrics Surgery Urology
New Brunswick	General Medicine Internal Medicine
Passaic	Surgery
Paterson	Cardiovascular Disease Internal Medicine
Trenton	General Medicine Internal Medicine Occupational Medicine Surgery
NEW MEXICO	
Albuquerque	Chest Disease
NEW YORK	
Albany	Anatomy Cardiovascular Disease Electrocardiography General Medicine Internal Medicine Obstetrics and Gynecology Pediatrics Public Health and Preventive Medicine Surgery

STATE	CATEGORY
NEW YORK (continued	
Buffalo	Anesthesiology Cardiovascular Disease *Dermatology* Endocrinology General Medicine Gynecology Internal Medicine Malignant Disease Obstetrics Physical Medicine and Rehabilitation *Psychiatry*
Cooperstown	Malignant Disease
Jamaica	Radioisotopes Radiology
Marcy	Psychiatry
New York	All categories except: Endoscopy *Ephebology* Ophthalmology and Otolaryngology
Ray Brook and Saranac	Chest Disease
Rochester	Pediatrics
Roslyn	Cardiovascular Disease
Thiells	Pediatrics
Welfare Island	Neurology Radiology
NORTH CAROLINA	
Asheville	*General Medicine*
Durham	General Medicine
Edenton	General Medicine
Morgantown	General Medicine
Rocky Mountain	General Medicine
OHIO	
Cincinnati	Clinical Pathology Obstetrics and Gynecology Occupational Medicine Otolaryngology *Pediatrics* Peripheral Vascular Radioisotopes Radiology
Cleveland	Cardiovascular Disease General Medicine Internal Medicine Ophthalmology *Physical Medicine and Rehabilitation* Urology
Columbus	Chest Disease Internal Medicine Neurology and Psychiatry Occupational Medicine Ophthalmology Orthopedic Surgery Pediatrics
Toledo	Anesthesiology Cardiovascular Disease
OREGON	
Portland	Ophthalmology Ophthalmology and Otolaryngology Otolaryngology
PENNSYLVINA	
Altoona	General Medicine
Erie	General Medicine
Philadelphia	Anesthesiology Cardiovascular Disease Chest Disease Dermatology Electrocardiography Endocrinology Gastroenterology
PENNSYLVANIA (continued)	
Philadelphia (continued)	General Medicine Otolaryngology *Pediatrics* Radioisotopes *Surgery*
Pittsburgh	Allergy Psychiatry
PUERTO RICO	
San Juan	Radioisotopes Radiology
RHODE ISLAND	
Warwick	General Medicine
SOUTH CAROLINA	
Charleston	General Medicine
Greenville	General Medicine
TEXAS	
Austin	Radioisotopes
El Paso	Dermatology Pediatrics Surgery
Ft. Sam Houston	General Medicine *Psychiatry* Surgery Urology
Houston	Allergy *Anatomy* Anesthesiology Cardiovascular Disease Clinical Pathology *Endoscopy* Fractures Gastroenterology General Medicine Gynecology Hematology Internal Medicine Obstetrics and Gynecology Ophthalomolgy Otolaryngology Pathology Physical Medicine and Rehabilitation Radioisotopes Radiology
Hunt	General Medicine
San Antonio	Fractures *General Medicine* *Ophthalmology* Surgery
Temple	Anesthesiology General Medicine Pediatrics Proctology
VIRGINIA	
Roanoke	Ophthalmology and Otolaryngology
VERMONT	
Burlington	Electrocardiography
WASHINGTON	
Seattle	Cardiovascular Disease *Electrocardiography* Internal Medicine Neurology Obstetrics and Gynecology Pediatrics Psychiatry Surgery
WISCONSIN	
Milwaukee	General Medicine Hematology Pediatrics

MEDICAL NEWS

ILLINOIS

Chicago

Postdoctoral Study in Statistics.—Awards for study in statistics by persons whose primary field is not statistics but one of the physical, biological, or social sciences to which statistics can be applied are offered by the department of statistics of the University of Chicago. The awards range from $3,600 to $5,000 on a 9 months' basis or $4,400 to $6,000 on an 11 months' basis. The closing date for application for the academic year 1960-1961 is Feb. 15, 1960. Information may be obtained from the Department of Statistics, Eckhart Hall, University of Chicago, Chicago 37.

Society News.—The following officers were elected to the Chicago Orthopaedic Society for the year 1959-1960; president, Dr. Newton C. Mead; vice-president, Dr. Carroll B. Larson; president-elect, Dr. Sidney Sideman; secretary, Dr. Jerome G. Finder; and treasurer, Dr. Ralph T. Lidge.——The Chicago Society of Industrial Medicine and Surgery elected the following officers: president, Dr. George J. Cooper; vice-president, Dr. Richard E. Heller; secretary, Dr. Bille B. Hennan; and treasurer, Dr. Charles M. Drueck.

Personal.—Dr. Nels M. Strandjord, assistant professor, department of radiology, University of Chicago, was appointed a James Picker Foundation scholar. Announcement of the appointment was made in Washington, D. C., by the National Academy of Sciences–National Research Council on behalf of the foundation. The appointment carries with it a grant of $4,000 to support Dr. Strandjord in his teaching duties and in his research on x-ray diagnosis of stomach cancers.——Dr. Loyal Davis, chairman, department of surgery, Northwestern University Medical School, received an honorary fellowship in the Royal College of Surgeons of Edinburgh, Scotland, July 23 at a convocation held during a meeting of the Canadian and British Medical associations in Edinburgh. Dr. Davis, the only surgeon from the United States to be so honored, received the honorary fellowship of the Royal College of Surgeons of England in 1955.

Prosthetic Education Program.—Northwestern University Medical School announced the launching of its prosthetic education program, reportedly the first facility of its kind in the Midwest. The official opening of the new program was marked by a reception July 30 in the Rehabilitation Institute of Chicago, where the school is located. The new school will operate on a training grant from the Department of Health, Education, and Welfare, Office of Vocational Rehabilitation. This is Northwestern's second government project in the prosthetics field. The first was the Prosthetic Research Center, established in 1956 by the Veterans Administration for developing new prosthetic devices and fitting techniques. The combined annual budgets of the two projects total $150,000. Courses in the new school will disseminate contemporary information about the prescription, fabrication, and fitting of artificial limbs and braces and the rehabilitation of the orthopedically handicapped. Twenty-one courses lasting from one to three weeks each will be offered during the academic year to physicians, prosthetists, therapists, and rehabilitation counselors. Directly responsible for the organization of the new program is its academic adviser, Dr. Clinton L. Compere, associate professor in orthopedic surgery at Northwestern. The program's director is J. Warren Perry, Ph.D., assistant professor of neurology and psychiatry.

NEW JERSEY

Meeting of Clinical Researchers.—On Sept. 16, the New Jersey Chapter of the American Federation for Clinical Research will meet at the Veterans Administration Hospital, East Orange. There will be a joint meeting with the section on experimental medicine and surgery, Academy of Medicine of New Jersey. Four papers are scheduled as follows:

The Pathophysiology of Dumping Syndrome, Dr. Bernard H. Chaiken, Short Hills.
The Medicolegal Aspects of Medical Research, Dr. William Furst, East Orange, president, New Jersey Neuropsychiatric Association.
T. P. I. in Related Tests, Dr. George H. Kostant, New York City.
The Effect of Smoking on Pulmonary Function, Dr. Edwin L. Rothfeld, Newark.

Each paper will be discussed following its presentation. Dr. Robert M. Pocelinko, Newark, is the secretary of the New Jersey chapter and Dr. Victor Parsonnet, Newark, is president.

Blood Bank in East Orange.—Ground will be broken in East Orange on Saturday, Sept. 12, for the Ballantine Memorial Essex County Blood Bank building, Dr. Kenneth E. Gardner, Bloomfield, president of the blood bank, announced. A $250,000 contribu-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

tion for the land and building, at Grove Street and Sussex Avenue, was given by P. Ballantine & Sons as a memorial to employes of Newark who gave their lives in service in World War II. This fund was set aside some years ago to be used as a memorial. The bank was organized in 1947, and there were 1,457 donors during the first year. The 1958 donor total was 17,170. The nine chapters of the American Red Cross recruit blood donors from the 22 Essex municipalities as well as from Kearny, Harrison, and Arlington. The 26 hospitals in the area use a total of about 30,000 units of blood a year, with more than half of this amount being provided through the Essex County Blood Bank.

NEW YORK

Symposium on Cinefluorography.—The second annual Symposium on Cinefluorography will be held Nov. 13 and 14, at the University of Rochester Medical Center. This symposium will emphasize the clinical and investigative value of cineangiocardiography; in addition, time will be provided for the presentation of information on image intensifier equipment, photographic technique and apparatus, and papers dealing with other clinical uses of cinefluorography. The program will begin with the "Second Annual Lecture on Cinefluorography of the University of Rochester School of Medicine and Dentistry," by Dr. Frank L. Campeti, who will summarize six years of clinical and experimental work on cineangiocardiography, and will review the indications and limitations of the method. Following this, a cardiologic team will discuss the diagnosis, prognosis, and surgical treatment of congenital and acquired heart disease. On Nov. 13, a panel of radiologists will extend this discussion to radiologic diagnosis. Cinefluorograms demonstrating will be shown that evening. The morning of Nov. 14 will be devoted to cinefluorographic equipment; motion-picture technique, including editing, print control, and special effects; cinefluorographic installations; and miscellaneous equipment, such as recording devices and injection apparatus. Saturday afternoon is reserved for the presentation of submitted papers dealing with previously unpublished information. Presentation of these papers will be limited to 20 minutes plus an additional 10 minutes for discussion. The deadline for the descriptions of cinefluorograms and abstracts of papers is Sept. 1. For information write Dr. George H. Ramsey, Chairman, Department of Radiology, University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, N. Y.

New York City

Fellowships in Endocrinology and Metabolism.—The availability of junior or senior fellowships in endocrinology and metabolism in the department of medicine, Cornell University Medical College, has been announced. These fellowships are to be designated the Ephraim Shorr Fellowships in Endocrinology in memory of Dr. Shorr, who for many years headed this section at Cornell. The fellows will be under the supervision of Dr. Ralph Peterson, associate professor of medicine. Stipends will be between $5,000 and $7,500 per year, depending on the number of years following graduation and the number of dependents. The deadline for applications is Oct. 15. Applicants should write for information to Dr. E. Hugh Luckey, Chairman, Department of Medicine, Cornell University Medical College, 1300 York Ave., New York 21.

Dr. Day to Go to Pittsburgh.—Dr. Richard L. Day, professor of pediatrics, State University of New York Downstate Medical Center, Brooklyn, was appointed medical director of Children's Hospital of Pittsburgh and chairman of the department of pediatrics at the University of Pittsburgh School of Medicine. Dr. Day will go to Pittsburgh in early 1960. He succeeds Dr. Edmund R. McCluskey, who resigned the two positions last year to become vice-chancellor for Pitt's Schools of the Health Professions. Dr. George H. Fetterman will continue to serve as acting medical director of Children's Hospital until Dr. Day arrives. Dr. Wayne H. Borges, associate professor of pediatrics will continue as acting chairman of the department of pediatrics until Dr. Day arrives. Dr. Day has been professor of pediatrics at Brooklyn since 1953.

Dr. Snyder Named College President.—Dr. Ralph E. Snyder, dean of New York Medical College, was elected president of the institution by the board of trustees. Dr. Snyder was appointed dean in 1953 and has functioned as chief executive officer of the institution since 1957. He will continue to hold the title of dean in addition to that of president. New York Medical College was founded in 1860, with William Cullen Bryant as its first president, and will celebrate its centennial with a year-long series of academic events beginning in the fall. As president of the college, Dr. Snyder is also head of Flower and Fifth Avenue Hospitals. He is also head of the New York Medical College–Metropolitan Hospital Center, the city's newest medical center composed of the college, Flower and Fifth Avenue Hospitals, Metropolitan Hospital, and Bird S. Coler Hospital.

NORTH CAROLINA

Annual Heart Symposium.—On Oct. 9, the 10th annual Winston-Salem Heart Symposium will be held at the Hotel Robert E. Lee. A panel discussion, "The Impact of Acute Metabolic Disorders on the Cardiovascular System," will be held in the morning, moderated by Dr. Philip A. Tumulty, Baltimore. Following the panel the following papers will be presented:

Practical Clues in the Interpretation of the Electrocardiogram, Dr. Marion Bryant, New York City.
Chronic Anti-Coagulant Therapy in Strokes and Heart Disease, Dr. Irving S. Wright, New York City.
Long-Range Management of Rheumatic Fever and Systemic Lupus, Dr. Tumulty.
Repair of Aneurysms—When and How?, Dr. Oscar Creech Jr., New Orleans.

A clinical pathological conference will be held at 4 p. m. A banquet is planned for 7 p. m. For information write the Forsyth Heart Society, Inc., 236 Nissen Building, Winston-Salem, N. C.

OHIO

Gift for Building and Endowment.—A 20-million-dollar gift from the Leonard C. Hanna Jr. Fund to Western Reserve University's School of Medicine and University Hospitals of Cleveland will be used for building and endowment purposes, according to officials of the two institutions. Each institution will receive 10 million dollars. Fund trustees said the gift was in recognition of the joint development program of the medical school and the hospitals. Chairman of the University Medical Center Development Committee is Mr. George M. Humphrey, former U. S. secretary of the treasury. Under his leadership the group hopes to raise 40 million dollars in the next 10 years to expand the joint facilities of the School of Medicine and University Hospitals. University President John S. Millis said that about 7 million of the 10-million-dollar gift designated for Reserve would go into the endowment fund to increase medical faculty salaries. The balance will go with matching federal funds to modernize the present medical school building and to erect an additional five-story structure. According to Dr. Millis, $1,300,000 of the matching federal funds have been received. Stanley A. Ferguson, director of University Hospitals, said that the 10 million dollars coming to his organization would be used for buildings and equipment. On Aug. 12, 1941, Leonard C. Hanna Jr. incorporated the Hanna Fund. He served as president of the board of trustees until his death in October, 1957. The group changed its name to the Leonard C. Hanna Jr. Fund earlier this year.

PENNSYLVANIA

Philadelphia

Lectures on Nutrition and Metabolism.—The Home for the Jewish Aged, in cooperation with the Committee on Nutrition and Metabolism, Philadelphia County Medical Society, and the National Vitamin Foundation, is sponsoring a series of lectures on nutrition and metabolism as they relate to specific medical problems of the aged, as follows:

Oct. 11—Dr. Robert W. Hillman, Brooklyn, "The Geriatric Patient—Nutritional Requirements."
Nov. 11—Dr. Herbert Pollack, New York City, "General Therapeutic Nutrition with Emphasis on Obesity."
Dec. 9—Dr. Richard W. Vilter, Cincinnati, "The Relation of Nutrition to Cardiovascular Disease."

PUERTO RICO

Dr. Vivas Named Dean.—Dr. Joseph R. Vivas was named dean of the University of Puerto Rico School of Medicine, San Juan, thus filling the vacancy created by the resignation of Dr. E. Harold Hinman on June 6. Dr. Hinman has accepted a position with the Public Health Division of the International Cooperation Administration. A 1934 graduate of the Medical College of Virginia, Dr. Vivas was director of graduate education at the Walter Reed Hospital in Washington from 1953 to 1957 and since that time has been chief of medicine and director of Gorgas Hospital in the Canal Zone.

TENNESSEE

Plan Medical Center Addition.—A three-story building providing expanded facilities for both radiological research and patient treatment will be the next addition to Memphis Medical Center. Dr. David S. Carroll, head, department of radiology, University of Tennessee College of Medicine and the City of Memphis Hospitals, said a portion of the space devoted to basic radiological research will permit the addition of personnel to the staff to expand the research program. The new building will be erected in the rear of the John Gaston Hospital. According to preliminary plans the new structure will connect to the Gaston Hospital and the out-patient clinic to the Gailor Hospital Building. The building, to be constructed and equipped at a cost of $1,500,000, will add 34,000 square feet to the Medical Center. The City of Memphis Hospitals is providing one million dollars, the University of Tennessee, $255,000, and the National Institutes of Health of the U. S. Public Health Service, $145,000.

WISCONSIN

Dr. Jacoby Named Anesthesia Head.—Dr. Jacob J. Jacoby, director of anesthesia, Ohio State University, Columbus, accepted an appointment at Marquette University School of Medicine, Milwaukee, as professor and head of the division of anesthesiology. The appointment was effective Aug. 1. Dr. Jacoby will be a full-time anesthesiologist at the Medical School and the Milwaukee County Hospital. His duties will be concerned with establishing a training program in anesthesiology for medical students and residents at Milwaukee County Hospital. By July, 1960, at least eight residencies in anesthesia will be available. Dr. Jacoby will also help to expand the already existing anesthesia program at the Veterans Administration Hospital, Wood, where he will serve as a consultant in anesthesia.

GENERAL

Meeting on Electrodiagnosis.—The sixth annual scientific session of the American Association of Electromyography and Electrodiagnosis will be held in Rochester, Minn., on Saturday and Sunday, Aug. 29 and 30. Those who wish additional information should write to Dr. Edward H. Lambert, Mayo Clinic, Rochester, Minn., Program Chairman.

Research Grants and Fellowships.—The National Institutes of Health, Public Health Service research center at Bethesda, Md., reported that 181 research grants and 232 fellowships totaling $4,471,475 were awarded during June. Of the month's total, $2,619,830 was allocated to support 288 new research grants and fellowship awards. The remaining $1,851,645 was for the continuation of 60 previously approved research grants totaling $1,450,766, and the continuation of 65 fellowships totaling $400,879. The new research grants were made to 89 institutions in 28 states, the District of Columbia, and 6 foreign countries. The new fellowships were awarded to 163 U. S. scientists and 4 scientists from other countries for study in 78 institutions in 29 states, the District of Columbia, and 6 foreign countries. Through the recently activated international postdoctoral fellowship program, the four fellowships were provided to investigators from Switzerland, Chile, Colombia, and the Netherlands.

Fellowships for Pediatric Residencies.—The recipients of the 1959 Wyeth Laboratories pediatric residency fellowships were announced by Dr. Philip S. Barba, Philadelphia, past-president of the American Academy of Pediatrics and chairman of the fellowship selection committee. The pediatric program, sponsored by the Wyeth Fund for Postgraduate Medical Education, provides a grant of $4,800 to each physician, thus enabling him to spend two years of advanced study in the care and the treatment of children. The 20 recipients, from 16 different states, are the second group to benefit from the program established last year by the Philadelphia pharmaceutical manufacturing firm. Selection was made on the basis of "interest in pediatrics, character, able performance of duties, and academic competence." The Wyeth fellowship winners may attend any hospital whose residency is accredited by the Residency Review Committee of the American Board of Pediatrics and the Council on Medical Education and Hospitals of the American Medical Association.

Northwest Proctologic Meeting.—The third annual meeting of the Northwest Proctologic Society will be held Aug. 27-29, at Timberline Lodge, Mount Hood, Ore. Two panel discussions are planned: "Urologic-Proctologic-Gynecologic Problems" and "Medical Management of Ulcerative Colitis," moderated by Drs. Lawrence Leslie, Eugene, Ore., and George Long, Portland, Ore. The program includes the following papers:

Cryptitis—A Study on Organisms Found, Dr. Howard K. Belnap, Ogden, Utah.
Coccygodynia, Dr. Guy E. Owen, Moscow, Idaho.
The Inoperable Fistula-in-Ano, Dr. E. D. Parkinson, Boise, Idaho.
The Large Long Bowel, Dr. Donald Laird, Portland, Ore.
A Technic for Marking the Mucosa of the Gastro-Intestinal Tract after Polypectomy, Dr. J. P. Sauntry, Seattle.
Use of Hypnosis in Proctology, Dr. Leslie.
Medical Management of Ulcerative Colitis, Dr. Long.

A general discussion, "The Irritable Bowel Syndrome," will be held the morning of Aug. 28. On Aug. 27, anorectal procedures are scheduled to be done at the Multnomah County Hospital, Portland. A banquet is planned for 7 p. m., Aug. 28. For information write Dr. John L. McKay, 645 Medical & Dental Building, Seattle 1.

Institute for Medical Society Management.—A practical "bread and butter" session on medical society organization, operation, and management, the 1959 Institute for Medical Society Management will be held at the Ambassador West Hotel, Chicago, on Wednesday, Aug. 19. The one-day program was designed primarily for presidents, presidents-elect, secretaries, executive-secretaries, and chairmen of policy boards of medical societies. Mr. Thomas A. Hendricks, Chicago, president, Medical Society Executives Association, will open the meeting to be followed by an address by Dr. Ernest B. Howard, Assistant Executive Vice-President, American Medical Association. Panel discussions will be held in six sections beginning at 11 a. m. At the 12:30 luncheon, Dr. Leonard W. Larson, Bismarck, N. D., chairman, Board of Trustees, American Medical Association, will present, "You, Leadership, and American Medicine." From 3:30 to 5 p. m., eight round-table discussions designed to discuss specific problems and exchange ideas and information will be held. The institute will precede the A. M. A.'s Public Relations Institute, Aug. 20-21. For information, write Mr. C. Lincoln Williston, Executive Secretary, Texas Medical Association, 1801 N. Lamar Blvd., Austin, Texas.

Group to Study Trichomoniasis.—Following the symposium on human trichomoniasis held at Rheims in May, 1957, a conference of international representatives was called under the chairmanship of Dr. Gaston Chappaz. This resulted in the formation of an international group to maintain interest and to pursue further studies in this field. The group has been constituted as a permanent commission under the auspices of the International Union Against the Venereal Diseases and the Treponematoses, with headquarters at Institut Alfred Fournier, Paris. The objectives of the study group are as follows: (1) To set-up an international registry of research workers especially interested in the field of human trichomoniasis. (2) To promote international scientific meetings. The first Canadian symposium on Nongonococcal Urethritis and Human Trichomoniasis will be held at Montreal, Sept. 21-22 (Secretary, Dr. Z. Gallai, 8580 Esplanade, Montreal 11, Canada). (3) To aid in the publication of original articles or their abstracts in the various foreign journals. (4) To assist the various research workers in contacting the many public and private organizations for grants. All research workers and other persons interested in this field are invited to become members of this organization by sending a curriculum vitae to Group International D'Etudes de la Trichomonase Humaine, Institut Alfred Fournier, 25 Boulevard St-Jacques, Paris XIV°, France.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	July 18, 1959		July 19, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	1
Massachusetts	1	1	..
Rhode Island	..	..	..
Connecticut	3	4	..
Middle Atlantic States			
New York	6	9	6
New Jersey	1	1	3
Pennsylvania	..	..	..
East North Central States			
Ohio	3	5	6
Indiana	3	3	1
Illinois	4	7	4
Michigan	2	6	4
Wisconsin	..	..	3
West North Central States			
Minnesota	5	5	2
Iowa	7	21	..
Missouri	20	32	2
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	6	8	1
Kansas	..	5	5
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	3
Virginia	5	8	5
West Virginia	4	6	1
North Carolina	6	6	2
South Carolina	1	1	..
Georgia	4	6	..
Florida	5	7	22
East South Central States			
Kentucky	..	..	1
Tennessee	12	12	5
Alabama	15	15	..
Mississippi	2	3	6
West South Central States			
Arkansas	8	11	1
Louisiana	3	5	1
Oklahoma	5	9	2
Texas	20	34	24
Mountain States			
Montana	..	..	3
Idaho	..	1	1
Wyoming	..	..	..
Colorado	2	2	1
New Mexico	..	4	..
Arizona	3	4	..
Utah	..	..	..
Nevada	..	1	..
Pacific States			
Washington	..	3	..
Oregon	4	5	..
California	6	7	7
Alaska	..	..	..
Hawaii	..	..	7
Puerto Rico	..	..	3
Total	166	257	133

Industrial Accidents.—Statisticians of the Metropolitan Life Insurance Company reported that gains in industrial safety have decreased the relative frequency of disabling work injuries in the United States by more than a third in 15 years. Last year's frequency rate for disabling injuries, as reported by the Bureau of Labor Statistics, was the lowest on record—29.4 per 1,000 workers, as contrasted with 45.7 per 1,000 in 1943. Accidents arising out of and in the course of employment in 1958 took 13,300 lives, while 75,000 persons suffered permanent physical impairment and more than 1,700,000 were disabled for at least one day after the day of injury. Industries vary greatly with respect to their work-injury experience, the statisticians point out. The logging industry had as many as 62.3 disabling injuries per million employee hours worked in 1957, and a moderately high ratio of deaths to injuries—nine deaths per 1,000 disabling injuries. The coal-mining industry had a lower frequency rate for injuries than in logging, but the proportion of fatal injuries was three times as great. Other industries with comparatively high frequency and mortality ratios are highway and street construction, other heavy construction, metal and nonmetal mining, and structural steel erection and ornamental iron work. The electric light and power industry, with only 5.5 disabling injuries per million employee hours worked, experienced 29 deaths per 1,000 disabling injuries in 1957—the highest ratio of deaths to injuries of any industry for which data are available. A low frequency and a comparatively high proportion of deaths to injuries is also found for workers in petroleum refining, in steel mills, and in the industrial organic chemical industry.

Yugoslavian Receives Rehabilitation Fellowship.—The World Rehabilitation Fund announced the creation of the Donald Dabelstein Memorial Fellowship and the awarding of the fellowship to Prof. Branko P. Bajić, of Yugoslavia. The fellowship was created to honor the late Mr. Donald H. Dabelstein, former assistant director for program, Office of Vocational Rehabilitation, Department of Health, Education and Welfare, who died Oct. 8, 1958. Announcement of the awarding of the fellowship to Professor Bajić was made simultaneously in Belgrade and New York. Professor Bajić is inspector of special schools in the Republic of Serbia and is head of the section for special education in the Serbian Pedagogic Society. Professor Bajić will begin his year's advanced training in special education for handicapped children in New York City in September. During the period of his fellowship he will also represent Yugoslavia at the eighth World Congress of the International Society for the Welfare of Cripples in New York City Aug. 29-Sept. 3, 1960. The World Rehabilitation Fund, Inc, is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped. Currently there are 71 trainees (57 physicians and 14 nonphysicians) from 35 different nations who receive long-term advanced training in the U. S. under the auspices of the fund. Its honorary chairman include Mr. Herbert Hoover, Mr. Harry S. Truman, and Mr. Bernard M. Baruch. Currently the World Rehabilitation Fund is providing fellowships for advanced study in the United States for three other Yugoslavians: Dr. Bosko Zotovic, Dr. Dobrosav Matijasevic, and Mr. Josep Karic, an occupational therapist.

Increase in Hospital Admissions.—Hospitals in the United States cared for 700,000 more cases last year than in 1957, the American Hospital Association reported. A total of 23,697,000 hospital admissions was reported in 1958 as compared with 22,993,000 in 1957. The information was compiled from questionnaires received from 6,786 hospitals in the continental United States. Births reported by the hospitals reached an all-time high of 3,742,000 babies born in 1958. Each day last year there were more than 1,300,000 patients and 48,000 newborn babies in hospitals. The hospitals reported total expenses of $7,133,493,000, of which $4,660,191,000 was for payroll. Total assets for all hospitals amounted to $15,470,017,000. The hospitals employed 1,464,829 personnel in 1958, an average of 111 personnel per 100 patients in voluntary short-term hospitals to 34 per 100 patients in nonfederal psychiatric hospitals. The voluntary short-term hospitals cared for 15,825,136 cases; the average patient stay in these hospitals was 7.4 days. An average of $29.24 a day was spent by these hospitals for the care of each patient, an increase of $2.43 over 1957. Patients in voluntary short-term hospitals paid an average of $1.28 a day less than it cost to care for them. Total income from patients in these voluntary hospitals in 1958 was $3,277,242,000, while expenses were $3,426,520,000. Patient income made up 92.6% of the total income of all these hospitals in 1958, as compared with 91.2% in 1957. The balance came from contributions, grants, and income from such sources as endowments. The average expenditure per day in 1958 for each patient in the nation's federal psychiatric hospitals was $10.61. In the voluntary psychiatric hospitals the average expense per patient day was $16.35; in the proprietary psychiatric hospitals, $17.66; and in the state and local governmental psychiatric hospitals, $4.11. More than 277,000 professional nurses worked full-time in hospitals in 1958. This included over 236,000 nurses as hospital employes and more than 41,000 private duty nurses. Almost 65,000 professional nurses served in hospitals on a part-time basis. More than half of all U. S. hospitals were voluntary hospitals operated not for profit by churches and nonprofit associations. Fifteen per cent were proprietary and 33% were operated by agencies of federal, state, or local government. The federal hospitals represented a little more than 6% of all hospitals. Short-term hospitals cared for 96% of the total admissions while long-term hospitals received 4%. However, 63% of the patients in hospitals each day were in the long-term hospitals.

LATIN AMERICA

Symposium on Atherosclerosis and Coronary Disease.—To celebrate the 15th anniversary of the foundation of the National Institute of Cardiology of Mexico, an International Symposium on Atherosclerosis and Coronary Disease will be held Sept. 20-24, at the institute. The opening ceremony will be attended by the Constitutional President of the United States of Mexico, Adolfo Lopez Mateos. The program includes the following round-table discussions: Epidemiology and Nomenclature; Physiology; Metabolism and Biochemistry; Electrovectorcardiography; New Contributions to Medical and Surgical Therapy; Coagulation and Thrombosis; Clinical Aspects (Etiology and Methods of Diagnosis). All communications will be simultaneously translated into Spanish, French, and English. Registration fee is $100 in Mexican currency. For information write the Instituto Nacional de Cardiologia de Mexico, Ave. Cuauhtemoc 300, Mexico 7, D. F., Mexico.

FOREIGN

International Cytology Conference.—An International Cancer Cytology Conference, sponsored by the Institute de Oncologia and the Ministry of Health, Madrid, Spain, the International Union Against Cancer, and the Pan American Cancer Cytology Society, will be held in Madrid Sept. 22-26, 1960. President of the conference is Dr. J. Sanz Ibañez, director of the Madrid National Cancer Institute, and vice-presidents are Dr. James E. Ayre, Miami; Dr. Edmund V. Cowdry, St. Louis; and Dr. J. H. Maisin, Louvain, Belgium. Dr. Angel Valle Jimenez has been appointed secretary general and Dr. Hubert deWatteville, of Geneva, Switzerland, is general program chairman. Represented on the advisory council are Austria, Belgium, Canada, Denmark, England, Germany, France, India, Israel, Italy, Russia, Sweden, Turkey, and the U. S. The conference will focus on cytology research and advanced methods of cancer control through early cytology diagnosis. A brochure is available for distribution to medical and scientific groups. For information write Miss Elizabeth L. Hughes, U. S. Corresponding Secretary, 3007 Salzedo, Coral Gables, Fla.

Space Medicine Congress in Rome.—The second World and fourth European Aviation and Space Medicine Congress will be held in Rome Oct. 27-31. The following subjects will be developed: (1) present methods and data for the psychosphysic selection of the flying personnel and previsions for the future: (2) occupational pathology of flying personnel, maintenance and improvement of its psychophysic efficiency; (3) advances in scientific research of space medicine. A proposal will be made for the foundation of a European Aeromedical and Space Medicine Association. Persons concerned with aviation and space medicine are invited to participate with scientific papers, preferably relating to the subjects of the meeting. A summary, not exceeding 250 words (in English or French) containing the results and conclusion of researches, and completed by the title, should be sent before Aug. 31 to: "Organizing Committee of Aviation and Space Medicine Congress, 2/A via Piero Gobetti-Rome."

CORRECTION

Conference on Medical Education.—In the item "Second World Conference on Medical Education" (Aug. 1, page 1697) under Medical News the dates of the conference should have been Aug. 30-Sept. 4.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. *Final date for filing application* was May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certificates, new and reopened, Part I, and requests for re-examination Part II are now being accepted. *Part I. Written.* Jan. 15, 1960. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1959. No applications can be accepted after that date. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Oral.* St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pathology: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Chicago, Oct. 9-11. *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application was March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: Chicago, Oct. 19-20; New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application is July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Oral examinations (Part II):* Chicago, Sept. 14-15; Seattle, Sept. 17-18; Baltimore, Oct. 19-20; Cincinnati, Nov. 9-10; Boston, Dec. 14-15; Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application was July 1. *Oral.* September. Final date for filing application was July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

ARMY

Personal.—Col. John H. Voegtly, M. C., was named executive officer to the Army surgeon general in Washington, D. C., replacing Col. Bryan C. T. Fenton, M. C., who was assigned as commanding officer, Martin Army Hospital, Fort Benning, Ga.

PUBLIC HEALTH SERVICE

Natural Fluoride Content of Water.—A new report entitled "Natural Fluoride Content of Communal Water Supplies in the United States," Public Health Service publication no. 655, may be obtained from the U. S. Government Printing Office, Washington 25, D. C. The water supplies of 1,903 cities and towns with a combined population of 7 million contain enough fluoride naturally to prevent most dental cavities. Communities in 43 states use water in which the decay-preventing fluoride occurs naturally. The fluoride found naturally in water is identical in its effect to the fluoride used in controlled fluoridation. The 1,800 cities now adding fluoride to the public water supply adjust the concentration to that found in many of the naturally fluoridated water supplies throughout the country, a concentration of 0.7 to 1.2 parts of fluoride per million parts of water.

Poliomyelitis Vaccine.—The World Health Conference on live poliovirus vaccine held in June at Georgetown University under the sponsorship of the Pan American Health Organization brought together a mass of data about the use of the live vaccine in many areas of the world, including Latin America, Africa, Poland, Czechoslovakia, Russia, Singapore, the Netherlands, and Great Britain. Great progress is being made with these attenuated vaccines, bringing closer to reality the possibility of a safe and effective vaccine of this type. The trials undertaken to date and which have involved large numbers of persons were made mostly in the developing nations. Children in these countries, unlike those in the United States and in other more developed nations, normally develop immunity at an early age because of the widespread occurrence of the poliovirus.

Accordingly, there is need for controlled studies in which, prior to inoculation, persons can be tested for antibody levels, immunized, retested, and the results evaluated on a scientific basis. Mass programs of immunization have provided encouraging but not as yet complete scientific data on which to base a real judgment as to the effectiveness of these live vaccines. To the degree that these mass immunization programs have possibly prevented poliomyelitis in nations where they have been used, the effort has been worthwhile. The Public Health Service will continue to follow the present studies and encourage others with interest and the hope that the result will be a vaccine that is easier to administer, one which may provide longer lasting immunity, and one which, presumably, could be produced at lower cost. To date, the Public Health Service has received no applications for licensing an attenuated virus vaccine. Should such an application be received, its division of biologic standards will exercise its responsibility for insuring that the product is safe, potent, and capable of commercial production.

Disability Days.—As a result of illness and injury, workers with family incomes under $2,000 a year lost an average of 10.3 days from work during the 12 months ending June 30, 1958, as compared with a loss of 5.9 days for those in families earning $7,000 and over. An inverse relationship existed also between income and other forms of restricted activity, such as days in bed due to illness and injury. Workers 65 years of age and over lost about 11 days from work compared with 8.4 days for those in the 45-to-64-year group and 6.3 days for those aged 17 to 44. City children lost 9 days from school, rural nonfarm children 7.8 days, and farm children 7.3 days, on the average, as a result of illness and injury. Farm children 15 and 16 years of age lost about 10 days from school as compared to 6.5 days lost by urban children of these ages.

This information appears in the latest of a series of published statistical reports issued by the U. S. National Health Survey. The data apply to the total civilian population of the country, exclusive of persons confined to long-term institutions. Respiratory illnesses as a group were the leading cause of restricted activity. They were responsible for 40% of all such restriction and 50% of all days in bed. The totals for this group of diseases were affected by the Asian influenza epidemic, but even in a normal year the respiratory diseases are likely to head the list. Circulatory diseases, including heart disease, ranked second in terms of total volume of disability, followed by injuries and their chronic effects, with digestive diseases running a close fourth.

The new publication contains additional statistics on the relationships between disability and various characteristics of the population. The data are derived from the continuing nationwide household interviewing with a representative sample of the population, conducted for the Public Health Service by the U. S. Bureau of Census. The report entitled "Disability Days, United States, July 1957-June 1958" (Public Health Service publication no. 584-B 10) is available from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 40 cents a copy.

future; (2) occupational pathology of flying personnel, maintenance and improvement of its psychophysic efficiency; (3) advances in scientific research of space medicine. A proposal will be made for the foundation of a European Aeromedical and Space Medicine Association. Persons concerned with aviation and space medicine are invited to participate with scientific papers, preferably relating to the subjects of the meeting. A summary, not exceeding 250 words (in English or French) containing the results and conclusion of researches, and completed by the title, should be sent before Aug. 31 to: "Organizing Committee of Aviation and Space Medicine Congress, 2/A via Piero Gobetti-Rome."

CORRECTION

Conference on Medical Education.—In the item "Second World Conference on Medical Education" (Aug. 1, page 1697) under Medical News the dates of the conference should have been Aug. 30-Sept. 4.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application was May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certificates, new and reopened, Part I, and requests for re-examination Part II are now being accepted. *Part I. Written.* Jan. 15, 1960. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1959. No applications can be accepted after that date. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Oral.* St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

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Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application was July 1. *Oral.* September. Final date for filing application was July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

of Physicians in 1954; member of the American Society of Biological Chemists, American Academy of Arts and Sciences, National Academy of Sciences, and the Société de Pediatrie de Paris; served as a member of the staff and head of the metabolism division of the Children's Hospital; held honorary degrees from Yale University, University of Zurich, and the University of Chicago; editor of the *American Journal of Clinical Investigation* from 1941 to 1947; died in the Massachusetts General Hospital May 28, aged 75.

Glackman, John Clay Ⓜ Rochester, Ind.; Chicago Homeopathic Medical College, 1904; served as chairman of the state board of health; veteran of World Wars I and II; city health officer and member of the city board of health; at one time health officer of Spencer County; died in St. Joseph's Hospital, Kokomo, May 21, aged 78.

Glinert, Mark, Brooklyn; Medizinische Fakultät, der Universität, Vienna, Austria, 1924; died in Bay Harbor, Fla., Feb. 3, aged 62.

Grosjean, Joseph C. Ⓜ Bay City, Mich.; Trinity Medical College, Toronto, Ont., Canada, 1900; past-president of the Bay County Medical Society; for many years vice-president of the Agricultural Life Insurance Company, of which he was medical director; on the honorary staff at Mercy Hospital, where he was a senior surgeon for many years; died May 14, aged 85.

Hajworonsky, George Juri, Cherokee, Iowa; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1947; interned at Columbus Hospital in New York City, where he served a residency; served a residency at St. Francis Sanatorium for Cardiac Children in Roslyn, N. Y., and State Mental Health Institute in Cherokee; died in Iowa City May 19, aged 39.

Harper, Sage Ⓜ Douglas, Ga.; Medical College of Georgia, Augusta, 1933; veteran of World War II; member of the American Academy of General Practice; died in the Douglas–Coffee County Hospital May 26, aged 51.

Hays, William Clarence, Sherman, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; died in Shands Hospital, New Albany, May 16, aged 77.

Hines, John Allen, Alabaster, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1921; served as a member of the county board of education; died in the Highland Baptist Hospital in Birmingham May 22, aged 62.

Holloway, Hosah Sellers Jr. Ⓜ Notasulga, Ala.; Tulane University School of Medicine, New Orleans, 1941; interned at the Charity Hospital in New Orleans; veteran of World War II; died March 14, aged 43.

Howard, Frank Davis, Birmingham, Ala.; University of Tennessee College of Medicine, Memphis, 1948; veteran of World War II; later served in the U. S. Air Force; interned at Jefferson Hillman Hospital in Birmingham, where he served a residency; served a residency at the Lloyd Noland Hospital in Fairfield and the Veterans Administration Hospital in Birmingham, where he was head urologist; died in Tarpon Springs, Fla., May 27, aged 34.

Hubbard, Ralph Waldo Ⓜ Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1932; veteran of World War II; captured by the Japanese and held a prisoner of war for 32 months; released March 29, 1945; continued service in the Army reserve, retiring with the rank of lieutenant colonel; upon retirement was awarded the Distinguished Service Cross; associated with the Hubbard Hospital, where he died May 19, aged 51.

Hudson, Frederick Auld Ⓜ Enid, Okla.; Northwestern University Medical School, Chicago, 1908; in 1920 president of the Garfield County Medical Society; founder of the Enid General Hospital; died May 17, aged 74.

Humphrey, Henry Martin Ⓜ Kirksville, Mo.; Barnes Medical College, St. Louis, 1899; died May 16, aged 84.

Ironside, Paul Allan Ⓜ Haddonfield, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1930; served on the staff of the West Jersey Hospital in Camden; died in London, England, May 21, aged 57.

Jackson, Greenleaf L., Nashville, Tenn.; Meharry Medical College, Nashville, Tenn., 1911; died in the Davidson County Hospital March 19, aged 69.

Johnston, Louis Campbell Ⓜ Chicago; Northwestern University School of Medicine, Chicago, 1911; fellow of the American College of Surgeons; served during World War I and was awarded the Silver Star for gallantry in action; on the staff of the Grant Hospital; died June 1, aged 71.

Jolley, James Frank Ⓜ Mexico, Mo.; Rush Medical College, Chicago, 1913; fellow of the American College of Surgeons; on the staff of the Audrain Hospital; died May 24, aged 71.

Kaminski, Karolina, Syracuse, N. Y.; Uniwersytet Jana Kazimierza Wydzial Lekarski, Lwów (Lemberg), Poland, 1927; served as senior psychiatrist for the Newark (N. Y.) State School; died April 9, aged 59.

Kinnard, George Potts, Newnan, Ga.; Jefferson Medical College of Philadelphia, 1922; veteran of World Wars I and II; died in the Newnan Hospital March 4, aged 59.

DEATHS

Buck, Ulysses Grant Ⓜ Rothville, Mo.; Keokuk (Iowa) Medical College, 1896; served as president of the school board; associated with the St. Francis Hospital in Marceline, where he died May 3, aged 92.

Fenlon, Robert Laurence Ⓜ Boulder City, Nevada; State University of Iowa College of Medicine, Iowa City, 1919; member of the staff of the Boulder City Hospital; died in Battle Mountain May 19, aged 72.

Fisher, Alfred Taylor, Brooklyn; Medico-Chirurgical College of Philadelphia, 1901; died March 27, aged 79.

Fisher, E. Moore Ⓜ Washington, D. C.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1904; fellow of the American College of Physicians and the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; consultant in neuropsychiatry, Board of Veterans Appeals, Veterans Administration; died in the Baker Memorial division, Massachusetts General Hospital in Boston May 31, aged 83.

Flanagan, George Ernest Ⓜ Myerstown, Pa.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1923; member of the American Academy of General Practice; veteran of the Royal Canadian Air Force; secretary of the Lebanon County Medical Society; a director of the Myerstown Bank & Trust Company; associated with the Good Samaritan Hospital in Lebanon; died May 24, aged 61.

Foster, L. Fernald Ⓜ Detroit; born in Phillipsburg, N. J., Oct. 10, 1891; University of Pennsylvania School of Medicine, Philadelphia, 1918; secretary of the Michigan State Medical Society for 23 years; in 1954 the society honored him for his many years of outstanding service to the society and to the medical profession; at one time chairman of the board of directors of the Cooperative Medical Advertising Bureau of the American Medical Association; in 1955 vice-president and since 1956 president of the Michigan Medical Service and was named medical administrator of the organization in 1957; a founder of Blue Shield and a member of the board of directors since 1939; served as secretary of the Bay County Medical Society, of which he was past-president; past-president of the Northwest Regional Conference; helped found the Michigan Heart Association and served as its vice-president and first secretary; started the Michigan rheumatic fever control program as a member of the board of directors of the Michigan Society for Crippled Children and Adults; helped found the National Conference on Medical Service and was its first president; veteran of World War I; specialist certified by the American Board of Pediatrics; certified by the National Board of Medical Examiners; member of the American Academy of Pediatrics; formerly practiced in Bay City, Mich., where he was on the staffs of the Bay City General and Mercy hospitals; on the courtesy staff of the Harper Hospital, where he died May 27, aged 67.

Fry, Harvey Murrell, Binghamton, N. Y.; Jefferson Medical College of Philadelphia, 1896; past-president of the Susquehanna County (Pa.) Medical Society; for many years practiced in Rush, Pa.; died in the Binghamton City Hospital May 22, aged 88.

Fuller, William Theophilus, Nashville, Tenn.; Meharry Medical College, Nashville, 1930; also a dentist; died in the Hubbard Hospital May 24, aged 71.

Fuqua, William Arthur Ⓜ Grandfield, Okla.; Medical Department of Tulane University of Louisiana, New Orleans, 1910; medical director and owner of the Grandfield Hospital; died in Wichita Falls, Texas, May 19, aged 79.

Gage, Arthur Tenney, Oxnard, Calif.; Tufts College Medical School, Boston, 1906; associated with the Redlands (Calif.) Community Hospital; past-president of the Redlands Rotary Club; died in the General Hospital, Ventura County, May 16, aged 75.

Gamble, James Lawder Ⓜ Boston; born in Millersburg, Ky., July 18, 1883; Harvard Medical School, Boston, 1910; since 1950 emeritus professor of pediatrics at his alma mater, where he was assistant professor of pediatrics from 1922 to 1929 and professor from 1929 to 1950; instructor of pediatrics at the Johns Hopkins University School of Medicine in Baltimore from 1915 to 1922; served as physician with the American Red Cross in France from 1917 to 1919; in 1955 received the John Howland Medal and Award from the American Pediatric Society, of which he was past-president; member of the American Academy of Pediatrics and in 1946 received its Borden Award; in 1950 received the Chapin Award of the Rhode Island Medical Society and in 1951 the Kober Award of the Association of American Physicians, of which he was a member; received the Moxon Award from the Royal College

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Ⓜ Indicates Member of the American Medical Association.

of Physicians in 1954; member of the American Society of Biological Chemists, American Academy of Arts and Sciences, National Academy of Sciences, and the Société de Pediatrie de Paris; served as a member of the staff and head of the metabolism division of the Children's Hospital; held honorary degrees from Yale University, University of Zurich, and the University of Chicago; editor of the *American Journal of Clinical Investigation* from 1941 to 1947; died in the Massachusetts General Hospital May 28, aged 75.

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Hays, William Clarence, Sherman, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; died in Shands Hospital, New Albany, May 16, aged 77.

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Howard, Frank Davis, Birmingham, Ala.; University of Tennessee College of Medicine, Memphis, 1948; veteran of World War II; later served in the U. S. Air Force; interned at Jefferson Hillman Hospital in Birmingham, where he served a residency; served a residency at the Lloyd Noland Hospital in Fairfield and the Veterans Administration Hospital in Birmingham, where he was head urologist; died in Tarpon Springs, Fla., May 27, aged 34.

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Jolley, James Frank Ⓜ Mexico, Mo.; Rush Medical College, Chicago, 1913; fellow of the American College of Surgeons; on the staff of the Audrain Hospital; died May 24, aged 71.

Kaminski, Karolina, Syracuse, N. Y.; Uniwersytet Jana Kazimierza Wydzial Lekarski, Lwów (Lemberg), Poland, 1927; served as senior psychiatrist for the Newark (N. Y.) State School; died April 9, aged 59.

Kinnard, George Potts, Newnan, Ga.; Jefferson Medical College of Philadelphia, 1922; veteran of World Wars I and II; died in the Newnan Hospital March 4, aged 59.

Kirk, Clair Bishop Ⓢ Mill Hall, Pa.; Jefferson Medical College of Philadelphia, 1908; associated with Lock Haven (Pa.) Hospital; died May 22, aged 75.

Kitchens, Herschell Monroe Ⓢ Waldo, Ark.; University of Tennessee College of Medicine, Memphis, 1914; died May 18, aged 72.

Knipe, William Hugh Wellington Ⓢ Katonah, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1903; specialist certified by the American Board of Obstetrics and Gynecology; life fellow of the New York Obstetrical Society; fellow of the American College of Surgeons; served in France during World War I; formerly on the faculty of the New York Post-Graduate Medical School and Hospital and the New York Polyclinic Medical School and Hospital in New York City, where he was associated with the Gouverneur Hospital; died May 28, aged 78.

Langs, Louis Ⓢ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1915; associated with Adelphi and Brooklyn Doctors hospitals; veteran of World War I; died in the Maimonides Hospital April 18, aged 66.

Liles, Lester McKesson Ⓢ Watsonville, Calif.; Western Reserve University Medical Department, Cleveland, 1898; a member of the city board of health; died in the Watsonville Community Hospital May 18, aged 85.

Lummis, Frederick Rice Ⓢ Houston, Texas; born in Houston Nov. 1, 1884; Jefferson Medical College of Philadelphia, 1913; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; clinical professor of medicine emeritus at Baylor University College of Medicine; past-president of the Harris County Medical Society; in 1945 named chairman of the city board of health; trustee emeritus at Rice Institute; the Frederick R. Lummis Medical Foundation was named for him; consultant, Methodist, St. Luke's Episcopal, Memorial, and St. Joseph's hospitals, and the Hermann Hospital, where he died May 24, aged 74.

MacIntyre, Reginald Walker, New York City; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1907; served on the staff of the New York Polyclinic Medical School and Hospital and Hospital for Special Surgery; died in St. Luke's Hospital May 31, aged 78.

McGovern, Joseph Dunn Ⓢ Wewoka, Okla.; University of Nashville (Tenn.) Medical Department, 1910; on the staff of the Wewoka Memorial Hospital; died May 19, aged 72.

McKean, Alexander C., Harlingen, Texas; Northwestern University Medical School, Chicago, 1903; coroner for the province of Saskatchewan for many years, and was health officer of the town of Rouleau, Sask.; served on the staff of the Providence Hospital in Moose Jaw, Sask.; died April 2, aged 82.

Meisel, Stephen Julian Ⓢ New York City; Schlesische-Friedrich-Wilhelms-Universitat Medizinische Fakultat, Breslau, Prussia, Germany, 1923; associated with St. Clare's Hospital; died in Mount Sinai Hospital May 15, aged 61.

Moffatt, George, Seattle; McGill University Faculty of Medicine, Montreal, Que., Canada, 1902; practiced in Donnybrook, N. D., and later at Crosby, N. D.; died May 26, aged 89.

Morgan, David Wendell Ⓢ Pittsburgh; Albany (N. Y.) Medical College, 1930; fellow of the American College of Surgeons; veteran of World War II; associated with the Western Pennsylvania Hospital; died May 21, aged 58.

Nash, Edwin Alexander Ⓢ Des Moines, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1904; author of "Random Rhymes and Poems for Home Folks"; died May 3, aged 84.

Norris, John Franklin, Stewartstown, Pa.; College of Physicians and Surgeons, Baltimore, 1900; veteran of World War I; served as superintendent of the Somerset County Home and Hospital for the Insane in Somerset; formerly on the staff of the State Hospital in St. Peter, Minn.; for many years associated with the Veterans Administration in Camp Custer, Mich., and Sheridan, Wyo.; died in Dallastown May 19, aged 87.

Parrish, Frederick Watson, Tucson, Ariz.; College of Physicians and Surgeons, Los Angeles, 1910; died May 18, aged 89.

Petitt, Percy A., Paola, Kan.; Kansas City (Mo.) Hahnemann Medical College, 1908; county health officer; served on the faculty of the University of Kansas School of Medicine in Kansas City, Kan.; member of the American Academy of General Practice; associated with the Trinity Lutheran Hospital in Kansas City, Mo., where he died May 22, aged 75.

Pinard, Pierre Romeo, Sioux Falls, S. D.; St. Louis College of Physicians and Surgeons, 1893; also a pharmacist; served as vice-president of the Charles Mix County Board of Health; died May 22, aged 89.

Raymond, Edwin Ⓢ Mount Vernon, N. Y.; Universität Bern Medizinische Fakultät, Switzerland, 1938; associated with Mount Vernon Hospital and the Cross County Hospital; died May 8, aged 51.

Robert, Harold Russell, Farmingdale, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1912; at one time on the staff of the Dannemora (N. Y.) State Hospital; died in the Veterans Administration Hospital, Northport, May 2, aged 70.

Rosenstiel, Mary L. Ⓜ Freeport, Ill.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; associated with Deaconess and St. Francis hospitals; died May 17, aged 79.

Salinko, Stephen S. Ⓜ Milwaukee; Maryland Medical College, Baltimore, 1901; veteran of World War I and the Spanish-American War; died May 19, aged 88.

Saylor, Howard Lee Ⓜ Huron, S. D.; Starling Medical College, Columbus, 1894; fellow of the American College of Surgeons; veteran of World War I; served as president of the Huron Chamber of Commerce and in January, 1952, received its Distinguished Service Medal; died in St. John's Hospital May 8, aged 85.

Schonwald, John De Witt, Oxford, Ohio; Jefferson Medical College of Philadelphia, 1909; past-president of the Ohio College Health Association; served as medical director of Miami University; died in Sarasota, Fla., May 2, aged 72.

Schwartz, Henry Jacques Ⓜ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1915; died March 15, aged 71.

Scott, George Vane, Jersey City, N. J.; College of Physicians and Surgeons, Baltimore, 1912; died in the Jersey City Medical Center May 17, aged 70.

Seligmann, Fred Siegfried, Forest Hills, N. Y.; Hessische Ludwigs-Universitat Medizinische Fakultat, Giessen, Hesse, Germany, 1914; specialist certified by the American Board of Dermatology and Syphilology; associated with New York University-Bellevue Medical Center and New York Skin and Cancer Hospital; died April 2, aged 69.

Shaddix, Arthur C., Beaumont, Texas; Chicago College of Medicine and Surgery, 1913; associated with Baptist Hospital of Southeast Texas and St. Therese Hospital; died May 20, aged 75.

Sharp, Milton Ragsdale, Granger, Texas; University of Texas School of Medicine, Galveston, 1902; past-president of the Williamson County Medical Society; city health officer; died May 21, aged 81.

Simmons, John Wesley Ⓜ Brunswick, Ga.; University of Georgia Medical Department, Augusta, 1905; served as secretary-treasurer of the Georgia Industrial Surgeons Association; past-president of the Alumni Association of the Medical Department of the University of Georgia; on the staff of the Brunswick Hospital; died May 9, aged 79.

Sismondo, Adele Margaret Ⓜ California, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1938; associated with the Charleroi-Monessen Hospital in Charleroi; died May 19, aged 48.

Stead, Jenny English Crozier, Glendale, Calif; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; served as a medical missionary in India, Persia, and Iran; died April 12, aged 83.

Stricker, Frederick David Ⓜ San Rafael, Calif.; Detroit College of Medicine, 1900; served as executive secretary and state health officer of the Oregon State Board of Health; formerly secretary of the Oregon State Medical Society; past-president of the State and Provincial Health Authorities of North America and the Western Branch of the American Public Health Association; practiced in Tucson, Ariz., from 1919 to 1921; veteran of World War I; following his retirement the Oregon Public Health Association awarded him a plaque for outstanding contributions as a health administrator and organizer; died May 26, aged 84.

Sulman, William Richard Ⓜ Hazleton, Pa.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1925; specialist certified by the American Board of Internal Medicine; member of the American College of Cardiology; fellow of the American College of Physicians; associated with Hazleton State Hospital and St. Joseph Hospital, where he died April 24, aged 59.

Thomases, Saul Ⓜ Stratford, Conn.; New York University College of Medicine, New York City, 1939; certified by the National Board of Medical Examiners; served on the staff of the Bridgeport (Conn.) Hospital; died in the Grace-New Haven Hospital in New Haven May 21, aged 53.

Tonkin, Harry Glenville Ⓜ Martinsburg, W. Va.; Baltimore Medical College, 1908; veteran of World War I; twice mayor of Martinsburg; died in Miami, Fla., May 30, aged 78.

Tshernoff, Leon, New York City; American University of Beirut School of Medicine, Syria, 1912; died March 27, aged 71.

Turner, John Wakeman, Greensboro, N. C.; Northwestern University Medical School, Chicago, 1908; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War I; retired from the Veterans Administration Aug. 2, 1950; died May 9, aged 78.

Turque, Irwin Lawrence, Brooklyn; Long Island College Hospital, Brooklyn, 1925; veteran of World War II; associated with the Long Island College Hospital and the Kings County Hospital; died in the Veterans Administration Hospital May 17, aged 58.

Vereker, Martin Francis Ⓜ Hamilton, Ohio; Medical College of Ohio, Cincinnati, 1902; served as a member of the city council and health commissioner of Hamilton; for many years vice-president and a member of the board of the Columbia Building & Loan Association; died in the Mercy Hospital May 4, aged 83.

Wack, Frederic Van Deursen Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1927; veteran of World War II; died May 27, aged 58.

Walson, Charles Moore Ⓜ Brigadier General, M. C., U. S. Army, retired, Washington, D. C.; born in Laurel, Del., Aug. 24, 1883; Jefferson Medical College of Philadelphia, 1906; at one time practiced in St. Louis, where he was on the faculty of St. Louis University School of Medicine, and an assistant to the city health officer; commissioned a first lieutenant in the medical corps of the U. S. Army in 1912, served as a surgeon with American forces in the occupation of Vera Cruz, Mexico, in 1914; during World War I was an assistant to the chief surgeon of the American Expeditionary Forces in France; after the war, was stationed in Germany; from 1922 to 1926, an executive officer and hospital inspector at Walter Reed Hospital; later assistant to the Seventh Corps Area surgeon at Omaha and surgeon at Fort Benjamin Harrison (Ind.) Station Hospital; from 1936 to 1939 chief of the Plans and Building Branch, Office of the Army Surgeon General in Washington; in 1940 Second Corps Area surgeon and in 1942 became surgeon of the First Army; promoted to brigadier general in 1945; in addition to Army assignments, lectured on vital statistics at Creighton University in Omaha, and on tropical medicine at Indiana University School of Medicine in Indianapolis; became administrator of the American Red Cross Blood Program for the Greater New York area upon his retirement from the Army in 1947; held the post until 1951, when he became consultant to the American Red Cross Blood Program in Washington, serving until 1953; in 1948 went to the Far East on a special mission for the Army Surgeon General; fellow of the American College of Surgeons; held the Legion of Merit; died in the Walter Reed Hospital May 14, aged 75.

Walters, Albert Gerald Ⓜ Detroit; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1921; served as diagnostician for the city board of health; died May 10, aged 60.

Warren, Arthur Bradley Ⓜ Hardwick, Vt.; University of Vermont College of Medicine, Burlington, 1912; veteran of World War I; on the staff of the Hardwick Hospital; died May 2, aged 73.

Warrick, Joseph D. Ⓜ Camarillo, Calif.; Chicago College of Medicine and Surgery, 1917; past-president of the Barker County (Kan.) Medical Society; served as health officer of Sharon, Wis.; staff psychiatrist at Camarillo State Hospital; member of the American Psychiatric Association; died in the Medical Arts Center Hospital in New York City May 4, aged 63.

Welsh, Harold James, Geneva, N. Y.; University of Buffalo School of Medicine, 1924; at one time on the faculty of Cornell University Medical College in New York City; served on the staffs of the Western State Sanatorium in Greenwood Mountain, Maine, and St. Vincent's Hospital in Erie, Pa.; died in the Geneva (N. Y.) General Hospital May 4, aged 61.

Wiggins, Dallas Bronson, Philadelphia; Temple University School of Medicine, Philadelphia, 1913; served on the staffs of the Mercy-Douglass Hospital and the Jefferson Hospital; died April 27, aged 73.

Williamson, Plummer Bridges, Jackson, Miss.; University of Nashville (Tenn.) Medical Department, 1901; served as health officer of Pearl River County; for many years on the staff of the Mississippi State Hospital in Whitfield; died in the University Hospital May 19, aged 84.

Willie, Edward Henry, Brooklyn; Howard University College of Medicine, Washington, D. C., 1921; died in the Kings County Hospital April 8, aged 74.

Wilson, Thomas, Wynne, Ark.; Memphis (Tenn.) Hospital Medical College, 1913; member of the American Academy of General Practice; past-president and vice-president of the state board of health; past-vice-president of the Arkansas Medical Society; veteran of World War I; associated with the Cross County Hospital, where he died May 7, aged 73.

Woldert, Albert Ⓜ Tyler, Texas; University of Pennsylvania Department of Medicine, Philadelphia, 1893; also a graduate in pharmacy; past-president of the Smith County Medical Society; served as city health officer; honorary member of the staffs of the Medical Center Hospital and Mother Frances Hospital; died May 13, aged 92.

Woods, Clarence Hubert, Long Beach, Calif.; Jefferson Medical College of Philadelphia, 1896; died in Claremont May 27, aged 87.

Wyatt, Wortham Ⓜ Winston-Salem, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1913; veteran of World War I; associated with the City Memorial Hospital, where he died May 3, aged 71.

Wynn, Joseph Henry Ⓜ Naperville, Ill.; Chicago Medical School, 1931; died in Hospital of St. Anthony de Padua in Chicago May 11, aged 59.

Young, Ferrin, Florala, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1909; died May 18, aged 70.

Zaletel, Rudolph Peter Ⓜ Chicago; Universita Karlova Fakulta Lékarská, Praha, Czechoslovakia, 1919; died in the Illinois Central Hospital May 10, aged 69.

FOREIGN LETTERS

AUSTRIA

Anemia Infantum Pseudoleukemica.—At the meeting of the Austrian Society for Pediatrics in Vienna on April 7, H. G. Weippl said that, although it was originally considered to be a separate disease entity, opinions on anemia infantum pseudoleukemica now differ between complete repudiation and recognition of it as a reactive syndrome. The speaker reported cases with typical changes, one of a child with anemia of prematurity (second phase, iron deficiency) and another of a child with alimentary iron deficiency anemia, both patients having hepatosplenomegaly and leukocytosis with an increase in immature cells. All symptoms disappeared with the administration of iron alone, thus showing that all the changes depended on the anemia. The concept of a reactive syndrome thus seems to be justified.

Bronchoscopy.—At the meeting of the Society of Physicians in Vienna on April 10, H. Jenny reported results of a series of 2,550 bronchoscopies. Of 140 patients who were subjected to bronchoscopic examination in 1957 carcinoma was visualized in 103, or 73%, and in 64% the diagnosis of carcinoma was confirmed by exploratory excision. These results were much better than those obtained in earlier years, because of greater experience with the method and improved instruments. A special indication is the suspected specific perforation of lymph nodes, which can be removed by adequate endoscopic suction, particularly in children. With early bronchoscopy excellent results may be obtained and dangerous complications prevented. Endoscopic examinations are also indicated in patients with pulmonary tuberculosis and in those with all types of chronic, unexplained, inflammatory changes in the lungs and air passages. The risk associated with the procedure is slight if it is performed with the aid of general anesthesia, provided a reliable anesthetist is available.

Acid-Base Balance and Peritonitis.—At the same meeting R. Kühlmayer stated that by analysis of the acid-base balance and the electrolyte structure it was established, in 27 patients, that peritonitis is regularly associated with a compensated or manifest metabolic acidosis. The degree of the acidosis depends on the extent, duration, and severity of the peritonitis and makes prognostic conclusions possible. These acidotic disturbances of metabolism may be observed in patients with peritonitis of various origins, and also in those with postoperative or perforation peritonitis associated with ileus. The disturbances of electrolyte structure, which consist in a reduction of the total electrolyte concentration in the plasma, and, therefore, hyponatremia, or occasionally hypopotassemia and hypochloremia, are the result of a loss of electrolytes due to deficient absorption of electrolyte-containing digestive juices from the upper portions of the intestines, as a sequela of intestinal paralysis.

At the second surgical clinic of the University of Vienna the correction of the metabolic acidosis in patients with peritonitis was accomplished with a combination of sodium bicarbonate and sodium lactate. With this compound it was possible to correct the metabolic acidosis within one or two days in patients who had peritonitis which had been controlled surgically, resulting in an improved general condition. The other electrolyte disturbances may be treated according to the usual principles. The prognosis of the surgically controlled peritonitis can be improved specifically by the correction of the metabolic acidosis. Osmotic nephrosis was rarely observed at the autopsy of patients in whom a therapeutic correction of electrolyte disturbances had been attempted.

Circumscribed Opacities in the Lung.—At the same meeting H. Kunz stated that the interpretation of roentgenograms of the lung is not, as a rule, difficult, with the exception of circumscribed opacities. With each such round focus one must first decide whether the process is benign or malignant. In a series of 759 patients who were admitted to the second surgical clinic of the University of Vienna 40 had round foci, and in 6 the condition was inoperable. In many cases valuable time was lost through expectant treatment, because of the erroneous assumption of tuberculoma in patients with a malignant tumor or in those with benign tumors who had been treated for tuberculosis for months or even years.

Fracture of Vertebrae in Patients with Tetanus.—At the meeting of the Austrian Society for Pediatrics in Vienna, on May 5, H. A. Lippert reported that compression fractures (partly multiple) of the middle thoracic vertebrae were observed immediately after the onset of disease in three of eight young patients with tetanus. Fractures of the vertebrae have been observed frequently after tetanus in juvenile patients, and the prognosis is favorable. Roentgenologic examinations should be performed before the patients get out of bed, since the post-tetanic vertebral changes are asymptomatic in most patients, and back pain and in-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

creased kyphosis may be observed only in severe cases. The speaker emphasized that vertebral fractures have not been reported after treatment of tetanus with muscle relaxants, but that vertebral fractures occurred in two patients with moderately severe tetanus who, according to Mollaret's scheme of treatment, had not been treated with curare. For orthopedic treatment exercises, bed rest, with the patient placed on a hard mattress in the prone position, and a body cast have been used. Roentgenograms of fractures occurring after electroshock therapy are identical with those of fractures occurring after tetanus. The condition must be differentiated from vertebral osteochondrosis and congenital platyspondylisis.

Hydramnios.—At the Meeting of the Society of Physicians in Vienna on May 22, R. Ulm stated that the genesis of the amniotic fluid and the causes of its abnormal increase are not fully understood. With the aid of radioactive isotopes it was found that the infant in utero drinks about 8 liters of amniotic fluid daily which, after absorption by the intestine, is returned to the mother through the placenta. If for any reason the infant is not able to swallow, or if the gastrointestinal passage is interrupted, then the amniotic fluid circulation is disturbed and hydramnios results. Clinical observations on 30,000 deliveries provided complete confirmation of these views. Observation of hydramnios should indicate to the obstetrician the possibility of an intestinal abnormality and the necessity of an immediate pediatric examination of the newborn infant, so that a lifesaving operation may be performed while the infant's condition is still good.

The diagnostic usefulness of reported hydramnios for the early diagnosis of complete occlusion high in the gastrointestinal tract was confirmed by H. G. Wolf. A hydramnios was recorded four times in five patients with duodenal atresia and only once in six patients with duodenal stenosis. Of 4 patients with atresias of the proximal jejunum it was estimated that twice the normal amount of amniotic fluid was present before birth, while in 63 who had occlusion of the distal gastrointestinal tract a hydramnios was observed only once, in a patient with meconium ileus. In 24 patients who had esophageal atresia with a lower esophagotracheal fistula hydramnios was found only once, and this fistula was permeable only with a capillary probe. Since the significance of an early diagnosis of acute abdomen in the newborn infant cannot be overemphasized, hydramnios of the mother that cannot be explained otherwise should be the cause of appropriate examination of the newborn infant.

O. Thalhammer stated that in the surprisingly large water exchange of the fetus the fluid is secreted, at least predominantly, by the prismatic amnion cells of the middle portion of the placenta. It is swallowed by the fetus, reabsorbed by the intestine, and passed on to the fetal heart by way of the mesenteric veins. In the arterial portion of the fetal circulation most of the water is carried back into the amnion by way of the umbilical arteries through the kidneys and urinary passages. This circulation starts with swallowing and renal function at the end of the fourth month. Disturbances anterior to the fetal heart are frequently associated with hydramnios, and the same applies to disturbances between the fetal heart and the circulation of the mother (diabetogenous fetal disease with fetal-placental endarteritis obliterans). Disturbances between the fetal heart and the orifice of the urethra are frequently associated with oligohydramnios. Disturbances anterior to the fetal heart may be due to other causes.

The speaker observed a child who died of congenital ascites on the first day of his life. Autopsy revealed peritonitis with extensive adhesions close to the mesenteric root, which caused congestion, still clearly visible at autopsy, of the veins peripheral to the adhesions. The otherwise healthy mother had observed a great increase in weight and in her circumference in the course of the last weeks of her pregnancy, and she had had hydramnios. Only one part of the obstructions in the mentioned route of the water is associated with hydramnios and with oligohydramnios respectively. There must be still unknown compensatory mechanisms. Only a few cases of hydramnios (3 of the 95 in the speaker's series) could be explained by obstructions in the digestive tract.

Epilepsy in Childhood.—At the meeting of the Society of Pediatricians in Vienna, on April 14, Dr. H. C. Groh stated that he had treated children who had various epileptic manifestations with a series of anticonvulsant drugs. Detailed diagnostic procedures were used to determine the predominant form of convulsion and the course of the disease. Special attention should be given to the frequency with which the attacks occur, the eliciting factors, the possibilities of cerebral injuries, familial factors, and peculiarities in the environment of the child. Primary extracerebral causes of seizures and space-filling intracranial lesions should be excluded. The electroencephalogram is important for the determination of the type of seizure. The selection of the proper drug is determined by the form of seizures, the frequency with which they occur, the hour at which they occur, and the toxicity and cost of the drug. It is not wise to change from one drug to another too soon, because many anticonvulsants become effective only after they have been used for some time. A gradually increasing dose should be used until the maximal effect short of intoxication is achieved.

For infrequent major and focal seizures in infants mephobarbital or phenobarbital was preferred. In those with more frequent seizures of these types, if barbiturates were ineffective, methylphenylethylhydantoin (Epilan), with or without a small dose of barbiturates; a combination of diphenylhydantoin and mephobarbital (Comital); Comital with phenobarbital; Epilan with phenylethylbarbital; or Epilan with phenobarbital was used. For minor seizures phenylchloroacetylurea was given to most patients but in those with a classic spike-and-wave electroencephalogram or those in whom this drug was ineffective trimethadione and paramethadione were used.

For petit mal attacks characterized by momentary loss of consciousness, in patients with classic spike-and-wave paroxysms, these same drugs were given but in older children, especially those who also had major seizures, these drugs were combined with barbiturates or hydantoins. If these combinations were ineffective phenylchloroacetylurea was given, and if this was also ineffective acetazolamine or caffeine was tried. For psychomotor seizures phenylchloroacetylurea or primidone and hydantoins were given. Lightning, nodding, and salaam convulsions presented a therapeutic problem. There was no preferred therapy. Primidone and phenobarbital were the most promising. Trimethadione and paramethadione were ineffective. If a patient had combined seizures the major seizures were treated first, preferably with primidone. Minor seizures were often influenced at the same time. Once the major seizures are under control, combination with other drugs may be of value. Average doses for the various age periods, determined empirically, have been tabulated and were given as a basis for dosage. Regular supervision of treatment is essential. This includes advice by the physician as to living routine, education of the child, and periodic leukocyte counts in order to recognize early allergic or toxic side-effects of the drugs. In patients in whom treatment seems satisfactory yearly electroencephalograms should form the basis for the prognosis. Reduction of the dosage and the final withdrawal of the drug may be considered after freedom from seizures for two or more years.

INDIA

Hyperpyrexia in Children.—Ghosh and Singh (*Indian Journal of Child Health.* vol. 8, April, 1959) treated 11 children who had hyperpyrexia (a temperature of 105 F [40.6 C] or more) and such neurological symptoms as unconsciousness, drowsiness, and convulsions, with a lytic cocktail. Treatment was started with an intramuscular injection of 50 mg. of chlorpromazine, the dose being less in younger children. This was followed immediately by an intravenous drip of 5% dextrose solution at a rate of 15 drops per minute; 1 to 1.5 cc. of a mixture containing 50 mg. of promethazine, 50 mg. of chlorpromazine, and 100 mg. of meperidine in 12 cc. of saline solution was injected into the drip tubing every 15 minutes. Six such injections were given. This was followed by an intravenous drip containing 150 mg. of promethazine, 150 mg. of chlorpromazine, 150 mg. of meperidine, and 200 mg. of thiamine in 900 cc. of 5% dextrose solution. This was allowed to flow at the rate of 15 to 20 drops per minute until the temperature came down to 101 F (38.3 C), when it was replaced by plain 5% dextrose solution. The cocktail was restarted, if there was a secondary rise of temperature, until the temperature again came down to 101 F. The rate of the inflow was increased to 25 or 30 drops per minute if the temperature did not come down quickly enough. Supportive therapy in the form of cortisone intramuscularly or prednisone by mouth was given to five patients, thyroid extract orally to two, and oxygen by a nasal catheter to three.

Specific therapy was started once the general condition after hypothermia improved. This treatment was designed to enable the autonomic nervous system to withstand the stress of hypothermia and thus overcome the risk of circulatory failure, which invariably occurred in the past when patients with hyperpyrexia and neurological involvement were treated only by surface cooling with ice, and when the general condition became worse and terminated in death as the temperature came down. In this series of 11 patients 7 survived. Of these six were normal when last seen and one had a neurological defect in the form of generalized rigidity and inability to speak. The temperature came down in all cases, the fall being dramatic in all but two. Ice packs were used only if the fall in temperature was slow. In those who survived the general condition improved as the temperature came down, restlessness diminished, and response to stimuli returned. None of the patients developed any pulmonary complications.

Tetanus in Children.—Matveyev and Paul (*Indian Journal of Child Health*, vol. 8, April, 1959) found that tetanus accounted for 1.65% of all admissions to the Children's Hospital in Delhi. The incidence of tetanus neonatorum was exceptionally high—38 of 279 newborn infants, or 14%. The highest incidence was in August, September, and October. This may have been due to conditions of temperature and humidity during these months being favorable to the multiplication and growth of Clostridium tetani and, to a certain extent, to the increased birth rate during these months. As infection in these cases usually occurs at birth, when the umbilical cord is cut, the incubation period of tetanus neonatorum was four to seven days. Most of these children came from areas of the city with poor sanitary conditions.

There was often a history of siblings also having suffered from tetanus, and in two families several children had been affected. In 35 of 38 cases of tetanus neonatorum deliveries had been conducted at home by untrained persons, with violation of the most elementary laws of asepsis. None had received antitetanus serum before admission. In the older children meningitis and such local conditions as regional lymphadenitis; peritonsillar, retropharyngeal, and alveolar abscesses; acute parotitis; and severe stomatitis had to be excluded.

Although an incubation period of less than 48 hours usually means an unfavorable prognosis, two children with an incubation period of less than 24 hours survived. There was no correlation between the severity of the disease and the state of nutrition and physical development of the child. Absence of vomiting in these patients was striking, none of the children vomiting even once. Increased perspiration, which is supposed to be characteristic of tetanus, was not observed in any. Of 47 patients 18 had cyanosis. Only two of these survived, and their cyanosis was slight. This is an unfavorable sign; its degree corresponds to the severity of the disease. Trismus was present in 41, opisthotonus in 23, and risus sardonicus in 15. The convulsions were tonic in 30, tonic-clonic in 16, and absent in 1. Cessation of tonic convulsions was a good prognostic sign and was observed from the 8th to the 22nd day of the disease. The umbilicus was normal in only 8 of the 38 who had tetanus neonatorum, the rest showing some evidence of umbilical infection. The principal complications were bronchopneumonia in seven patients and stomatitis, due to moniliasis or secondary infection, in five.

Nasal feeding was used in most patients in the early stage. Oral feeding was started when the general condition improved, usually in the second week. Antitetanus serum was given to all the children, the dose varying from 40,000 to 300,000 I. U. It was given either as a single dose or in a course of injections. The effect of the serum administration was not closely related to the time of its administration after the onset of the disease. Thus, all the 14 children who received it on the first day died; 18 got it on the second day and 2 of these recovered; and 6 got it on the fourth day and 4 recovered. The effect depended more on the severity of the disease and was of help in subacute cases. As anticonvulsant therapy paraldehyde injections, phenobarbital orally, and chloral hydrate rectally were administered in early cases but were found to be unsatisfactory. Injections of paraldehyde and antibiotics were abandoned, since they disturbed the patients. Instead sedatives were given orally or rectally and the broad-spectrum antibiotics orally. Preparations of chlorpromazine and prednisolone were used to increase the sedative and relaxant effect and to combat toxemia and hyperpyrexia. The mortality was very high—34 of the 47 died.

Infantile Scurvy.—Although children of parents in a low income group live on cereals and insignificant amounts of milk, with hardly any supplement of fresh fruits or vegetables, frank scurvy is not so common as would be expected. Manchanda and Gupta (*Indian Journal of Child Health*, vol. 8, April, 1959) analyzed a series of 25 patients aged 7 months to 5 years who had frank scurvy. All were from very poor families. Three were breast fed, 5 received human and cow's milk, 4 got only cow's milk, 11 got a mixed diet, and 2 got cereals only. The diet of the mothers of the breast-fed babies was grossly inadequate during both pregnancy and lactation. All had a history of some illness in the preceding three to four months. Common misdiagnoses included caries of the spine, rheumatic arthritis, acute poliomyelitis, acute osteomyelitis, acute leukemia, paraplegia, and anemia. Sixteen had moderate and nine severe anemia. The characteristic radiologic signs of scurvy were seen more easily in the lower extremities than in the upper. Treatment consisted of 250 mg. of ascorbic acid given intramuscularly twice a day and 60 to 120 cc. of fresh orange juice, for varying periods. Results were good in all patients except one who had hepatic failure and jaundice and who died four days after admission. Improvement was evident in the others three to eight days after starting treatment.

Effects of Alcohol and Nicotine on Hypertension.—Gour and Mital (*Current Medical Practice*, vol. 3, April, 1959) investigated the reasons for advising patients with hypertension to restrict the use of alcohol and nicotine by studying this relationship in four groups of chicks. The first group served as controls. In the second group hypertension was induced by substituting 0.9% sodium chloride solution for drinking water. The third group received 50% alcohol, after hypertension was induced with salt, and the fourth consisted of chicks with salt-induced hypertension who were exposed to tobacco smoke. The normal range of systolic pressure in the control group varied between 112 and 136 mm. Hg and of diastolic between 92 and 116 mm. Hg. The total plasma cholesterol level in this group varied between 102 and 118 mg.% and the plasma lipid phosphorus level between 7.3 and 8.4 mg.%. The ratio of total cholesterol to lipid phosphorus was 14:1. In the second group the maximum level of systolic pressure was 168 mm. Hg and of diastolic 140 mm. Hg. The values for total plasma cholesterol (C), lipid phosphorus (P), and the C:P ratio, however, were unchanged in spite of the raised blood pressure. In the third group the blood pressure was a little lower than in the second group but the other values were unaltered, and there was no evidence of atherosclerosis in any of the chicks when they were killed after 24 weeks of observation. In the fourth group neither the blood pressure nor the blood chemistry was any different from that seen in the second group, and on autopsy no atherosclerotic changes were detected after 24 weeks of study.

Internal Carotid Thrombosis.—Ramamurthi and Rao (*Journal of the Indian Medical Association*, vol. 32, May 1, 1959) stated that thrombosis of the internal carotid artery is a much more common condition than is suspected. Many cases diagnosed as cerebral vascular disease are instead caused by occlusion of carotid arteries. The difficulty in diagnosing this condition is due to the variety of symptoms that may be manifest. The authors observed eight patients with thrombosis of the internal carotid artery, only three of whom showed the classical symptoms of ipsilateral blindness with contralateral hemiplegia. Three of the eight patients had papilledema, two had ocular palsy, three had mental disturbances, and two did not have any weakness of the contralateral limbs. The age of these patients varied between 11 and 55 years. The right side was involved in six cases and the left in two. One patient had a frank frontal lobe syndrome of mental disturbance. Five of these patients were treated with arterectomy, resection of the superior cervical ganglion, and in one ligation of the internal jugular vein, with a view to improving the cerebral blood supply.

Self-sufficiency in Drugs.—India's drug production in 1958 was nearly twice that of 1957. If the present rate of expansion continues India should be self-sufficient by the end of 1961 in the production of most raw materials or basic substances required for the pharmaceutical industry. It is thus expected that importation of drugs will be greatly reduced in the foreseeable future.

Carcinoma of the Uterus.—D. B. Reddy and coworkers (*Journal of the Indian Medical Profession*, vol. 5, March, 1959) found that although the incidence of carcinoma of the body of the uterus is low as compared with other malignant tumors of the genital tract, it has been rising. Of 34 cases observed by them since 1954, 10 were encountered during the last year alone. The average age of the patients in this series was 45 years (range 20 to 70). About 40% were in the age group 20 to 40. All the patients in this series except one were married and had borne one or more children. This does not correspond with the usual belief that cancer of the body of the uterus is more common in the unmarried and nulliparous. Most of the lesions were confined to the endometrium and myometrium. Early diagnosis and surgical treatment are therefore beneficial in these cases.

Leprosy.—At the annual general meeting of the leprosy workers' association the chairman said that the terror of the disease had definitely decreased. Compulsory segregation is fast being abolished, and the leprosy patient is no longer inevitably linked in the public mind with a leprosarium; 72 leprosy centers have been established, covering a population of over 8,500,000 and treating about 100,000 patients.

Birth Weight.—Mukherjee and Biswas (*Journal of the Indian Medical Association*, vol. 32, May 16, 1959) studied 1,054 consecutive births to determine the influence of the period of gestation, the sex of the infant, parity and age of the mother, and the socioeconomic status on the birth weight of the infant. The gestation period was calculated from the first day of the last menstrual period. The duration of pregnancy among the patients studied ranged between 7 and 11 lunar months, and most of the births took place at 39 to 41 weeks, when the average birth weight was 6 to 7 lb. (2,721 to 3,175 Gm.). The average birth weight for the entire series was 5.96 lb. (2,060 Gm.). A progressive increase in the birth weight was noticed, as the gestation period advanced, from a minimum of 2.06 lb. (1,160 Gm.) to a maximum of 6.59 lb. (2,925 Gm.).

The rate of increase was not uniform throughout the range of variation of the gestation period. It increased rapidly with gestation up to 35 weeks, after which it showed a decline. For the shorter periods of gestation male infants were slightly lower in weight than female infants in corresponding periods of gestation, but after 38 weeks they gained more weight than their female counterparts. The average birth weights varied between 5.67 (2,600 Gm.) for the first parity and 6.36 lb. (2,860 Gm.) for the eighth parity. The average birth weight showed a tendency to rise systematically with parity up to the fourth order, but the pattern of variation among higher parities was not systematic. The minimum age of the mother in this study was 14 and the maximum 44 years. Most of the mothers were in the age group 25 to 30. The average birth weight in the 14-to-18-year-old mothers was 5.5 lb. (2,190 Gm.) and in the 21-to-25-year-old mothers was 6.23 lb. (2,835 Gm.). Up to the age of 25 years there was a tendency for the birth weight to increase systematically with the mother's age. At higher ages a reverse tendency was noticed, the birth weight diminishing with advancing age.

Most primiparas were between 18 and 21 years of age. A systematic increase in the birth weight with the mother's age was noticed in the primiparas up to the age of 30 years. Among the group of para 2 and para 3 women a systematic increase in birth weight with the mother's age was seen, up to the age of 25 years, followed by a gradual but consistent decrease with advancing age. The pattern of variation of birth weights with respect to age was more or less the same for different gravidas. The birth weights of babies from higher socioeconomic groups were consistently higher than those coming from a lower class, for all periods of pregnancy. A larger proportion of the poorer mothers had extremely short periods of gestation, which also contributed to the reduction in the average birth weight of their babies to a significant extent.

Tuberculosis Association of India.—Presiding over the 20th annual meeting of the tuberculosis association of India in New Delhi, A. Kaur said that though in a welfare state the main responsibility for health services lay with the government, humanity would be the poorer if men and women had no opportunities to fulfill their desire to help their fellow men. Welfare organizations were therefore in a key position to provide for such aspects of human needs as could not be adequately covered by government agencies. The tuberculosis seal sale campaign has helped to make the public more conscious of the tuberculosis problem, but the campaign has not maintained the steady progress which was anticipated. The situation should be studied to find out how this drive could be intensified and made the real pivot of a whole nation's movement against tuberculosis.

Effect of Drug on Avoidance Response.—Sinha and Acharya (*Indian Practitioner*, vol. 12, March, 1959) stated that tranquilizing drugs such as Rauwolfia alkaloids and chlorpromazine disrupt a well-established conditioned avoidance response, which is not due to disturbance of motor coordination. They studied the blocking effect of reserpine and chlorpromazine and the facilitating effect of methylphenidate and epinephrine on conditioned avoidance responses in rats to find out whether the former decreased and the latter increased the rate of conditioning. The animals were trained during a preliminary period of 10 days so that the avoidance response was fully established. The four drugs were given on different days to groups of animals according to a counterbalanced sequence of drug order to exclude any effect of the drug previously used, and placebos were included to serve as controls.

The drugs were given intraperitoneally, and sufficient time was allowed after administration for the peak effect of the drug to develop. This time was three hours for reserpine, two and one-half hours for chlorpromazine, one and one-half hours for methylphenidate, and one-half hour for epinephrine. The animals were then subjected to the conditioned stimulus. A determination of the specific drug effect on these responses was made on five consecutive days. Reserpine and chlorpromazine definitely depressed and blocked the avoidance responses, while methylphenidate and epinephrine increased them. With placebos the responses were maintained at a constant level. The response developed under one drug could be altered by administering another. All these drugs acted on the conditioned avoidance responses in a specific manner, while leaving the unconditioned responses unaffected. Epinephrine enhanced the response from 65 to 100% and methylphenidate from 40 to 100%. Reserpine blocked the response from 30 to 0% and chlorpromazine from 10 to 0%. With placebos a constant response of 33% was obtained.

A New Antimalarial Drug.—A. P. Ray and co-workers (*Journal of the Indian Medical Association*, vol. 32, May 16, 1959) studied the efficacy of 377-C-54, a naphthalene derivative that has shown a high degree of activity against avian and simian plasmodia, against human malaria under rural and urban conditions in 124 patients (70 with vivax and 54 with falciparum malaria). Thick and thin smears were made for detecting the parasite. At least 100 fields of the thick film were examined before submitting a negative report. Three dosage schedules were tried: (1) 200 mg. twice a day on the first and once a day on the second day, a total of 600 mg.; (2) a single dose of 400 mg.; and (3) a single dose of 600 mg. The first schedule was used in urban hospital patients and the other two in home treatment in rural areas. Blood smears were collected daily to determine the rate of clearance of asexual parasites from the peripheral circulation, which was taken as the main criterion of the activity of the drug. In hospital patients 92.3% of those with vivax malaria became afebrile within 48 hours, while relief of clinical symptoms in all patients could be recorded only after 72 hours.

The response in those with falciparum malaria was not so good; 55.5% became afebrile within 48 hours, 77.7% within 96 hours, and the rest took as long as five days. Parasite clearance was 100% in those with vivax malaria within 48 hours. In those with falciparum malaria it was 55.5% within 48 hours and 100% only after 96 hours. With a single dose of 400 mg. clearance of asexual parasites was 61.1% in those with vivax malaria within 24 hours and 94.4% within 48 hours. It took 72 hours for parasite clearance to occur in 100%. Corresponding figures for those with falciparum malaria were 64.7%, 82.3%, and 96 hours. The response, however, was remarkably prompt with the single dose of 600 mg. In those with vivax malaria parasite clearance was 97.4% within 48 hours. In those with falciparum malaria the rings had disappeared in 67.5% within 24 hours and in 100% within 48 hours. Thus the therapeutic response was variable with different plasmodia. With the divided dosage schedule its action against Plasmodium vivax was comparable to that of chloroquine. The response was much slower against Plasmodium falciparum with this dosage. The drug is therefore unsuitable in divided doses for patients with this type. The response with a single dose of 600 mg. was comparable to that with chloroquine. The drug was on the whole well tolerated.

NETHERLANDS

Influenza Pandemic.—In the *Nederlands tijdschrift voor geneeskunde* (103:1098, 1959), M. F. Polak reported the results of his analytic studies on morbidity and mortality in the Netherlands influenza pandemic of 1957. One-third to one-half of the population was affected. The first cases were observed in the southeast of the country, and within four weeks the whole country was involved. There were 1,230 deaths or 11.2 per 100,000 inhabitants. The areas affected early showed a higher death rate (14.1) than the regions affected later (10.4). This was probably due to the lower morbidity in the areas affected later. The 20-to-29-year-old age group showed the lowest death rate (3.0). With increasing age this rate increased; in the group of those aged 80 and above it was 171.2 per 100,000.

During the epidemic there was a decrease in mortality among younger people and an increase in that among older age-groups. In general, women showed a higher death rate than men up to the age of 40, but above that age the death rate was higher in men. On the average the death rate was lower in large towns (7.7) than in villages (14.5). The reason for this difference is not clear. There was no difference in morbidity between towns and villages.

Of the 1,230 who died 799 had a preexistent disease. The occurrence of such a disease was most frequent among older people, reaching 82% in the group of those aged 70 and above. The intercurrent diseases most often encountered were oligophrenia, multiple sclerosis, paralysis agitans, valvular heart disease, tuberculosis, kyphoscoliosis, and diabetes. In the 20-to-39-year-old age group the mortality among pregnant women was more than twice that among nonpregnant women (8.0 and 3.8 respectively). In addition to the deaths directly due to influenza an approximately equal number of deaths were reported in the same period. These additional deaths were mostly in persons in the highest age groups, who died of respiratory and circulatory diseases. Influenza was probably a contributing factor in these cases.

Pulmonary Changes in Influenza.—After the 1918 influenza pandemic some observers reported certain pulmonary changes which were thought to be the direct result of this disease. Later the relationship between such anatomic changes and the influenza virus could be proved by the presence of antibodies against this type of virus. P. de Baan (*Nederl. tijdschr. geneesk.* 103:721, 1959) studied 10 patients who died of influenza in the 1957 pandemic. The same changes were seen again, although more frequently and to a more pronounced degree. This was thought to be partly the result of the present role of antibiotics, which in many instances prevented secondary infection. The frequent occurrence of these lesions was ascribed to certain pneumotropic properties of the virus involved.

On macroscopic examination the lungs of these patients showed hemorrhagic areas with well-defined lobular limitations. On microscopic examination the main characteristics appeared to be degeneration, necrosis, and desquamation of the epithelial cells at all levels of the bronchial tract. This was followed by a vigorous regeneration which was most pronounced in the terminal bronchioles and in the respiratory bronchioles of the first and second order. In the alveoli the degeneration was accompanied by a hemorrhagic and fibrinous effusion. In the central areas of some alveolar lesions thrombosis of the capillaries was seen. This resulted in complete necrosis within about two weeks. In other areas, however, the capillaries remain open. In such instances signs of regeneration of the alveolar cells were seen. The peculiar character of the changes in the epithelial cells all along the bronchial tract warranted the conclusion that the virus could invade not only the bronchial epithelium but also the most peripheral alveolar cells. The author stressed the relationship between the alveolar effusion and the often severe cyanosis and dyspnea observed in patients suffering from this disease. Furthermore, this explains the high death rate in patients with a preexistent heart disease.

Persons Aged 100 and Above.—According to the central bureau for statistics there appeared to be, on Jan. 1, 1959, 58 persons (22 men and 36 women) who were 100 years old or older (in a population of about 11 million). Of these 27 were exactly 100 years of age and one was 109. Among these persons there were no married couples.

NORWAY

Pathogenic Staphylococci in Hospitals.—Since 1949 Prof. T. M. Vogelsang has been studying the behavior of staphylococci in response to penicillin medication. In his latest report (*Tidsskrift for den norske laegeforening*, May 1, 1959) he stated that tests were made in 1958 to determine whether the use of antibiotics other than penicillin might replace it and thereby reduce the frequency of penicillin-resistant strains. The author concluded that if the examination is made early in an epidemic, it may be possible to show that only one or two persons are carriers of the strain causing the epidemic. If they are patients they must be isolated, and if they are members of the hospital staff they should be temporarily suspended. Since so many persons are intermittent carriers, there is a good chance of the epidemic strain's disappearing from the upper respiratory tract during residence outside the hospital.

Epidemic Hepatitis.—Since infectious hepatitis was added to the list of reportable diseases about 17 years ago, 106,982 cases have been put on record, with an annual fatality of more than 2,000 in recent years. Early in 1956 an outbreak in a rural community 40 miles from Oslo inspired the public health authorities to send Dr. T. Bjerkedal (*Tidsskrift for den norske laegeforening*, May 1, 1959) to study it. He visited 1,042 persons in 273 homes. Of these 156 (15%) gave a history of jaundice at some earlier date. Suspicion fell on a 34-year-old man who, in the autumn of 1955, had infectious hepatitis under conditions peculiarly favorable to its spread to persons whose water supply was downstream of the river to which he had had access. In many cases, however, the disease must have spread by direct contact. The comparative immunity enjoyed during the present outbreak by persons with a record of jaundice at an earlier date suggested that infectious hepatitis often confers a lasting immunity. The author concluded that sanitary control of water supplies could do much to prevent future outbreaks. His optimism was more guarded with regard to the prevention of infection by direct contact, because the disease may be infectious before it has become patent, by virtue of the jaundice it provokes.

Iron in the Marrow.—At the Halden City Hospital Serck-Hanssen and Breck (*Farmakoterapi*, vol. 1, 1959) stained 40 sternal marrow smears from 23 patients having various forms of anemia with potassium ferrocyanide. Their objectives were (1) to discover a simple method for demonstrating stainable iron in sternal marrow, (2) to explore the possibilities of a semiquantitative grouping of the preparations, and (3) to learn whether there is any correlation between the quantity of stainable iron in sternal marrow and the patient's anemia, as estimated by the usual hematological criteria. In their opinion the most important outcome of this test was its ability to demonstrate the absence of stainable iron in a smear. When this is the case, treatment with iron is indicated. In their 23 patients in whom iron was demonstrable in this way iron medication was ineffective. Although no definite upper or lower limit could be put to the iron content of marrow, the quantity of such iron often varies with the hematological picture. Therein lies the diagnostic value of this test.

UNITED KINGDOM

Conan Doyle Centenary.—The centenary of the birth of Conan Doyle (1859-1930), the doctor who created Sherlock Holmes, fell on May 22. He studied medicine at Edinburgh University and after spending six months as a ship surgeon and another six months as an assistant, he settled in general practice at Southsea, where in eight years he never earned more than $1,200 a year. Yet he had a good knowledge of medicine, as in his novels he describes extra systoles, edema due to fibrillation, angina pectoris, aneurysms, rheumatic valvular disease, and left ventricular failure with orthopnea, with careful adherence to medical probabilities. During these eight years he was writing profusely and many of his stories were published, although many were also returned. He never earned more than $200 a year from writing during this period. He left Southsea in 1890 to study ophthalmology in Vienna. On his return he settled in Devonshire Place, London, where most of the Sherlock Holmes stories were written. He soon gave up medicine for writing, although he served as a doctor in the South African war in 1899, and wrote the history of the campaign. In 1902 he was knighted. Conan Doyle continued to write until 1926, when the last of the Sherlock Holmes stories appeared. He died in 1930.

At a Conan Doyle centenary exhibit in London is an original letter from Paul Ehrlich expressing his interest in the writer and asking for a signed portrait. Ehrlich's request was granted and the portrait of Doyle always hung in his study. Other interesting exhibits are the *Strand* magazine with the first of the Sherlock Holmes stories, and an illustrated program of the dramatic version staged in New York in 1900 with William Gillette as Holmes.

Institute of Diseases of Chest.—The existing laboratories of the Institute of Diseases of the Chest proved inadequate for the research work that is being done there and a new building to accommodate the research departments has been built on the grounds of the Brompton Hospital for Diseases of the Chest, London. The institute has become a highly important center for training research workers and consultants in clinical medicine, particularly diseases of the chest. Important clinical advances by Dr. Neville Oswald and laboratory advances by Dr. Lynne Reid are being made in the study of bronchitis. Research in cancer of the lung and the biochemistry of cellular respiration by polarographic techniques is also being done.

Radiation Induced Cancer.—Eight more cases of radiation-induced cancer were described by Garrett (*Brit. M. J.* 1:1329, 1959). At first this was seen only in x-ray or radium workers, but in recent years cases have occurred in patients who have had radiotherapy for the treatment of benign as well as malignant conditions. All these cases were of laryngeal and pharyngeal carcinoma occurring in women who had had thyrotoxicosis treated by local irradiation of the thyroid gland many years earlier. The longest latent interval was 44 and the shortest was 20 years. According to Garrett a latent period of 44 years is probably the longest on record for a radiation-induced carcinoma of the larynx. In most of the patients described, the skin over the neck showed the stigmata of irradiation although in one, the first indication of a laryngeal lesion was pain in the throat and dysphagia. Carcinoma of the larynx and pharynx is not common in women, and if a woman has symptoms referable to these organs she should be asked whether her neck was treated with irradiation many years before.

Myocardial Infarction and Plasma Lipoprotein.—Dodds and Mills studied the lipoprotein pattern of blood at short intervals in 78 patients during a period of two months after myocardial infarction (*Lancet* 1:1160, 1959). Samples were taken when possible within 24 hours of the attack, three to four hours later, and thereafter at intervals of seven days. The average age of the patients was 58 years. The lipoprotein patterns were compared with those of 220 healthy men of the same age using ultracentrifugation, Cohn fractionation, and paper electrophoresis. The results showed that a myocardial infarction is itself associated with a pronounced lipoprotein abnormality, which is manifest for at least two months after the attack. The total plasma cholesterol and percentage of cholesterol in the β-lipoprotein of the blood was much above the normal figure, and the cholesterol in the α-lipoprotein was significantly lower. The atherogenic index was also elevated. These observations support the well-known hypothesis that coronary artery disease is associated with a high plasma cholesterol, low α-lipoprotein cholesterol, and high atherogenic index. Unfortunately, it was not possible to determine the lipoprotein levels before the attack of infarction. If these abnormal levels are present before an attack it is suggested that such estimations might be used to distinguish those who will contract coronary artery disease from those who will not. It seems probable from their data that myocardial infarction in men younger than 45 years of age is often preceded by detectable lipoprotein abnormalities which became more evident after the attack, whereas in the elderly it is more common to find the acute disease in men with normal lipoprotein patterns. The authors concluded that the blood lipoproteins were, in some patients, concerned with the development of coronary artery disease and that the infarct itself had an effect on the lipoprotein pattern.

Radiotherapy and High Pressure Oxygen.—A new unit for the application of radiotherapy to cancer patients breathing oxygen under high pressure, while anesthetized in a special chamber, was built at St. Thomas' Hospital in London. Cancer cells are more susceptible to the effects of radiation at high oxygen concentrations. A few years ago a preliminary trial was made of the effects of irradiating cancer tissue in patients breathing pure oxygen under three or four atmospheres of pressure. The investigation was temporarily abandoned when convulsions occurred in some of the patients. These have now been shown to be preventable by conducting the procedure with the patient under anesthesia. This provides the added advantage of keeping the patient still and free from apprehension. The new unit consists of a treatment room, control space, anesthetic room, laboratory, and staff room. The cobalt unit consists of two identical 2,000-curie cobalt-60 teletherapy heads mounted opposite each other. Fixed on rails in front of it is the pressure chamber. The monitoring apparatus includes an ECG; a microphone to follow respiration; a pneumotachograph which measures the flow, tidal volume, and minute volume of the respiratory gases; a plethysmograph to indicate the limb blood flow; apparatus for the automatic recording of blood pressure and temperature, including that in the chamber; an encephalograph for measuring the depth of anesthesia; and a polarograph for measuring tissue-oxygen tension.

Hereditary Alactasia.—A hitherto unrecognized congenital abnormality, an inability to hydrolyze lactose, was described by Holzel and co-workers (*Lancet* 1:1126, 1959). They observed two breast-fed siblings who failed to thrive, although their intake of milk was adequate. Lactose and glucose-plus-galactose absorption tests showed that glucose and galactose were readily absorbed by both infants, but that lactose was not. The ingestion of the latter did not lead to any significant increase in the blood level of monosaccharides, which is observed in normal infants. Since lactose is not normally absorbed as such but is hydrolyzed by intestinal lactose into glucose and galactose it was inferred that the specific lesion was a failure to hydrolyze lactose. As lactose is the only carbohydrate in any quantity in milk and constitutes 40% of the total caloric value, inability to utilize this sugar would explain the failure to gain weight. The infants gained weight when cereal and glucose were added to the feedings. As the enzyme defect occurred in siblings it was considered that the condition might be hereditary and the term hereditary alactasia was suggested for it.

New Androgen.—Clinical trials with a new androgen, fluoxymesterone, were described by Buckle (*Brit. M. J.* 1:1378, 1959). This is about 10 times as potent as methyltestosterone as it is active in oral doses of 2 to 4 mg. daily. The steroid was given to 10 patients; 2 of whom were eunuchs, 7 eunuchoids, and one of whom had pituitary infantilism. The potency of the drug was assessed on a subjective basis and the results compared with those obtained previously with methyltestosterone administered by mouth. None of the patients showed any sign of androgen deficiency while under treatment. Fluoxymesterone was fully effective when taken orally. It was no more active when given sublingually. Androgens have salt-retaining properties and it might be expected that fluoxymesterone, being a hydroxy-substituted steroid, would probably show this property to an exaggerated degree, but there was no evidence of edema.

Status of the Family Doctor.—In a research pamphlet issued by the Fabian Society, which is Socialist inspired, Dr. Bruce Cardew, the general secretary of the Medical Practitioners Union and editor of *Medical World*, strongly objected to family doctors having their offices in their homes. He believed very few houses are suitable for this as it constantly involves the doctor's family in the affairs of the practice. Most houses are limited in size and this determines how the doctor should practice medicine. There is seldom room for partners or additional staff. Patients become attached to a particular house and do not wish to go elsewhere with the result that the longer a doctor practices from his home the more difficult it is for him to move. The patient cannot help comparing the equipment and attention received in a modern hospital with that in the office of the family doctor, and consequently the status of the physician whose office is in his home is lowered in the eyes of his patients. From the doctor's point of view such an office has much in its favor. It is cheaper, it reduces traveling time, and patients become attached to the home and the wife as well as to the doctor, so that if a new doctor comes the patients continue to attend. At present 80% of family doctors practice from their homes.

Far too many doctors are forced to lower their clinical standards because they are ill-equipped and have not the time to practice good medicine. If they had fewer patients to care for, were better housed, better organized, and in closer touch with other health and welfare agencies, they could give their patients more attention, could relieve the hospitals of much of their work, and would reduce much of the sickness benefit now paid out from national insurance funds.

In 10 years, only 10 health centers for group practice by doctors have been built. In these centers 100 physicians serve 100,000 patients. Dr. Cardew states that in terms of achievement, health centers must be said to have failed. He hopes that the next Labor government will set aside enough money for experiments with health centers so that more experience may be gained. While experiments with health centers continue, other ways must be found of improving standards of general practice. From the doctor's point of view group practice is the more attractive. It is based on a voluntary association of members with a common aim. It enables groups to select their points of practice, to plan the layout of the buildings to their own requirements, and to choose their own secretaries and receptionists. The doctors own and control their practices and cannot be interfered with.

Suggested Ban on Boxing.—In its editorial of June 6 the *Lancet* advocated the total abolition of boxing by law because of the health hazards attached to it. Deaths continue to occur in the ring, usually from gross injury to the brain or its vessels. A young boxer, who had a wife and children, recently died in Windsor Hospital after being knocked out in an amateur tournament, and a welterweight champion, aged 24, incurred an intracranial hemorrhage. Time and again it has been stressed that the path of boxing can lead to brain damage, imbecility, blindness, and death, yet nothing is done to stop it. On the contrary, official bodies such as the British Broadcasting Corporation extend the spectacle on television to ever-widening audiences, inclusing young children. According to the *Lancet* 64 deaths, including 22 in amateurs, in four years is a heavy price to pay for a sport which makes the brain its chief target.

The medical case against boxing is now so strong that doctors have a clear duty to fight for its total abolition, but they would have to contend with the vested interests concerned, with the strong and thoroughly unhealthy, though largely subconscious, public appetite for violence and bloodshed, and with the indifference of the public. It is suggested that one or more of the medical bodies in Britain should follow the Belgian example of persuading the government to pass stringent legislation against boxing before television audiences see some unsuspecting youth battered to death in the ring. Asked about the possible ban, the British Medical Association stated that it had no official policy in the matter. The medical officer of the British Boxing Board of Control said that most stringent regulations had been drawn up and that before a boxer was issued a license he had to pass stiff medical tests. His health and career were carefully watched from the time he put on his boxing gloves. Everything humanly possible was done to safeguard his health. Unless fit, he was not allowed to fight. From the point of view of an insurance hazard, boxing is classified with basketball and ice hockey and is rated as less dangerous than American football, polo, or even scull rowing.

Tuberculosis in the Elderly.—Pulmonary tuberculosis is increasingly becoming a disease of older persons, and particularly of men over 65 years of age. The number of reported cases in men over this age has almost doubled in the last 16 years. Mass radiography surveys show that the yield of active tuberculosis cases is 7 per 1,000 examined in those over 60, compared with 4.37 per 1,000 examined in persons under this age. It is generally thought that tuberculosis in older persons is a very chronic disease, but according to Smith some older persons have a clear chest film and then subsequently develop active tuberculosis (*Brit. M. J.* 1:1448, 1959). In a series of 100 persons over the age of 55 years diagnosed by him as having pulmonary tuberculosis 49 had had a previous chest film taken when they were more than 45 years old. The first film of 23 of these 49 patients, or 46%, showed no evidence of intrapulmonary disease, and many of them had been radiographed within five years of diagnosis.

It, therefore, seems that a clear chest film in an older person is of limited value only. If there is any suspicion of pulmonary tuberculosis in those in the older age group it is, thus, essential to radiograph the chest, even if a fairly recent film had been reported clear. Certainly radiological reports of "bronchitic changes" and "unresolved pneumonia" should be regarded with suspicion from the point of view of both tuberculosis and lung cancer. Many so-called new cases of tuberculosis in older people are due to breakdowns of old lesions regarded as inactive on previous radiographic examination. Reactivation of lesions not radiologically visible also occur.

What is not generally realized is that, contrary to the usual course of events, younger members of a household may infect the older ones. Regular mass surveys of older persons are advocated, although it is notoriously difficult to persuade them to submit to this. Lassitude, anorexia, and loss of weight, too often regarded as normal features of advancing years, may be the only symptoms of pulmonary tuberculosis in the elderly. Cough, if it occurs, is frequently attributed to "bronchitis" or smoking. Smith advised that the appearance of the above symptoms, with or without pulmonary involvement, calls for radiographic examination of the chest, even if a recent film had been reported clear.

Cross-Infection in Hospitals.—Cross-infection due to antibiotic-resistant strains of Staphylococcus pyogenes phage type 80 is now a matter of concern in many hospitals. A hospital epidemic due to this organism was described by Williams and co-workers (*Brit. M. J.* 1:1374, 1959). Swabs taken from wounds, the anterior nares and the skin of patients, and from the nares of hospital staff members were cultured. Blankets were also examined for bacterial contamination. Primary infection of the skin causing boils and furuncles in adults, and conjunctivitis and pemphigus in the newborn, accounted for 46% of all infections and 53% of those due to Staph. pyogenes phage type 80. Cross-infection of wounds and secondary infection of the respiratory tract caused most of the other cases. Nearly 15% of healthy nurses were infected on the skin and 51% were nasal carriers. Over 30% of the medical staff had positive nasal swabs. Nearly all operative wounds were found to be free from infection for the first few days, but many became secondarily infected with tetracycline-resistant Staph. pyogenes phage type 80. Cross-infection with tetracycline-resistant staphylococci phage type 80 was also found to be frequent in the hospital outpatient department.

Attempts at wholesale elimination of the infection were undertaken. Walls, ceilings, floors, and furniture were washed with an antiseptic-detergent mixture, and all utensils were steam sterilized or disinfected. Blankets were disinfected, hands washed with hexachlorophene soap and treated with 1% chlorhexidine hand cream, and nasal carriers treated intranasally with 0.5% neomycin ointment for a month. Carriers among the patients were bathed three times daily. In spite of these measures, they failed to reduce the incidence of cross-infection, although the carrier rate was reduced. It was impossible to isolate all carriers. Widespread infection of a hospital with such a resistant strain leads to increased risks to patients admitted for any reason and to increased septic lesions in the nurses. Failure to reduce cross-infection was attributed largely to increased foci of infection with Staph. pyogenes phage type 80 and other tetracycline-resistant strains in general practice. Ideally, persons so infected should be identified before hospitalization and then isolated.

Breast Cancer.—A new approach to the treatment of breast cancer has been made by Watson and Turner, who treated a series of 34 patients by the simultaneous administration of testosterone and thio-TEPA, an antimitotic alkylating agent known to be lethal to the cells of breast cancer (*Brit. M. J.* 1:1315, 1959). Oophorectomy was also performed before treatment in premenopausal patients. To one group an aqueous solution of 15 mg. of thio-TEPA was given intramuscularly two or three times a week until the leukocyte count fell below 3,000 per cubic millimeter. Treatment was then stopped and resumed when the leukocyte count returned to pretreatment levels. Another group received 30 mg. of thio-TEPA on alternate days until a total dose of between 180 and 300 mg. was given, depending on the response and leukocyte counts. After the completion of this course the patient rested for three to six weeks and then a similar course of treatment was given. Some patients were put on a maintenance dose of 15 to 30 mg. of thio-TEPA at intervals of two to four weeks; 200 mg. of testosterone propionate was given intramuscularly five times a week, beginning one week before the course of thio-TEPA therapy and continuing for two weeks after its completion. Six patients with pleural and peritoneal effusions had 30 mg. of thio-TEPA instilled directly into the cavity after paracentesis in addition to their normal course of intramuscular injections. Adjuvant therapy such as transfusion with concentrated erythrocytes for anemia or cortisone for thrombocytopenia was given when necessary.

Only those patients with widely disseminated lesions or with recurrences after radiation or operation were so treated. Before commencing treatment a clinical, radiologic, and hematological survey was made, and estimations were made of the presence of C-reactive protein, sedimentation rate, plasma proteins with their electrophoretic pattern, blood uric acid level, alkaline phosphatase level, and daily urine calcium level. Progress was recorded every 14 days. Tumor masses were measured and visible lesions were photographed. Simple mastectomy was performed on 11 previously untreated patients.

The most satisfactory results were obtained in those patients receiving both thio-TEPA and testosterone. Marked inhibitory effects were obtained in 30 patients, that is in 88%, which compares favorably with the accepted figure of 33% for treatment with testosterone alone. There was some evidence that testosterone protects normal marrow and normal growing tissues against the depressive action of thio-TEPA, which can then be given in larger doses. The authors suggested that a compound might be made incorporating the ethylenimino group of thio-TEPA with testosterone. They stated that the clinical, histological and radiologic evidence of destruction of malignant cells obtained in the advanced cancers of their series pointed to the possibility of completely eradicating a tumor and its metastases by chemotherapy. They believed that a wider use should be made of chemotherapy as an alternative to radiation in the treatment of breast cancer. They advocated a trial of surgery and chemotherapy instead of surgery and irradiation.

CORRESPONDENCE

ARCHIVES OF ERRORS

To the Editor:—The Council on Clinical Chemistry of the American Society of Clinical Pathologists has established an *Archives of Errors* for the accumulation and dissemination of errors in leading textbooks and journals relating to clinical pathology. Most persons in the practice of clinical pathology are aware that corrections of published errors pertaining to laboratory tests are often not published by textbooks and journals. The Council on Clinical Chemistry hopes to accumulate a list of some of these errors for distribution to people working in the laboratory so that they can profit by the mistakes and corrections of others.

Letters were written to the authors of leading textbooks on clinical pathology asking their reaction to such a program; the response was enthusiastic. To date, errata sheets on two textbooks have been made available; one is Annino's "Clinical Chemistry: Principles and Procedures" (Boston, Little Brown & Company, 1956), and the other is Knight and others' "Ultramicro Methods for Clinical Laboratories" (New York, Grune & Stratton, Inc., 1957). Pathologists and people working in laboratories will supply data on errors which they have noted and corrected in books and journals. These methods can then be made available to other people working in the field. At present, if a report of error is received by the editor, it is forwarded immediately to the author for checking. If the author concurs, the correction is sent to the office of the American Society of Clinical Pathologists for publication in its bulletin. Through the cooperation of all people working in clinical pathology, this program can be expanded into a useful, central clearing house for the benefit of all physicians.

Persons having information on errors and pathologists interested in working with the committee as part of the program should contact the editor of the *Archives of Errors.*

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MICROSCOPIC HEMATURIA

To the Editor:—In a widely circulated recent brochure the statement was made that the centrifuged urinary sediment may normally contain 4 to 10 red blood cells per high-power field. It was the immediate reaction of urologists in our department that this figure was too high and that if it were taken as normal many significant lesions in the urinary tract would be missed. A review of the subject of microhematuria was then undertaken in an effort to determine the number of red blood cells per high-power field considered to be within normal limits by most authorities.

Inspection of the standard textbooks in laboratory diagnosis, urology, and internal medicine revealed remarkably few statements as to the exact number of red blood cells permissible in the normal centrifuged urinary sediment. Thomas Addis states in his book "Glomerular Nephritis: Diagnosis and Treatment" (New York, The Macmillan Company, 1948) that "we should see nothing or next to nothing in the volume inspected on a quantitative slide unless renal disease, and disease of a certain intensity, is present. Now and again it might happen that we come across a red cell, or even, conceivably a hyaline cast in a normal urine, but that accident would only make it necessary that we go farther and look at several unit volumes."

Greene, at the Mayo Clinic, found that, in a group of patients with asymptomatic microscopic hematuria with 1 to 10 red blood cells per high-power field, 55% had a definite abnormality in the urinary tract, such as hemorrhagic cystitis, renal calculi, or a bladder neoplasm.

On the basis of a medical-actuarial impairment study conducted by the New York Life Insurance Company in 1951, it was found that the mortality increases in direct proportion to the number of red blood cells in the urine. If there are more than five red blood cells per high-power field the mortality is increased sufficiently to warrant increasing the premium for these life insurance applicants.

It is the opinion of those interested in diseases of the urinary tract and in laboratory diagnosis at the University of Michigan Medical School that more than one red blood cell per rare high-power field in a routine centrifuged urinary sediment must be considered abnormal. This is the value that the sophomore medical students are taught in their course on clinical microscopy. We believe that any patient with more than one red blood cell per rare high-power field on repeated urinalyses should have a complete urologic investigation, even in the absence of urinary symptoms.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Value of Electrocardiography When Coronary-Artery Disease Is Suspected. J. W. Todd. Lancet 1:845-848 (April 25) 1959 [London].

Electrocardiography cannot help in deciding whether or not a patient has anginal pain of effort. It is of small or doubtful value in determining both causation and prognosis when anginal pain is present. When a patient gives a history of attacks of precordial pain of an indeterminate character, electrocardiography is sometimes of considerable help. In differentiating between emotional cardiac symptoms and anginal pain of effort, the electrocardiogram is valueless. When cardiac infarction is suspected, electrocardiography gives unequivocal guidance if the characteristic electrocardiographic changes of recent infarction are present. But the electrocardiogram reflects only imperfectly the gravity and extent of the process in the heart, and a normal electrocardiogram cannot exclude infarction. Used routinely, electrocardiography may enable insurance companies to refuse to insure life, or enable employers to refuse someone employment. It is useless to the person concerned and, by bringing to light minor abnormalities, may make it possible for an unwise physician to turn the person into an invalid. The interpretation of electrocardiograms is often difficult, there being great variation between the reports of different experts on the same tracing, and considerable variation in the reports of the same expert on the same tracing at different times.

These considerations suggest that electrocardiography has been greatly overvalued in the investigation of patients with suspected coronary-artery disease. There are 2 main reasons for this overvaluation: 1. Because fatal and severe coronary-artery diseases are both undeniably important, one tends to assume the importance of determining whether or not a patient has minor coronary-artery disease. The presence of such disease neither provides a good reason for giving treatment nor enables an accurate prognosis to be made. Because the importance of the problem is exaggerated, the importance of the means which is thought to solve it, i. e., electrocardiography, is exaggerated in turn. 2. Among all the machines used for diagnosis, the electrocardiograph is the most impressive, but the readings supplied by the machine are useful only when interpreted by man, and this interpretation is not always simple. Even if in diagnosing cardiac infarction the electrocardiographic evidence alone is superior to the other evidence alone, in practice all the available evidence should be considered together.

Reduction of Serum Cholesterol Levels and Beta-Lipoprotein Cholesterol Levels by Nicotinic Acid. W. B. Parsons Jr. and J. H. Flinn. A. M. A. Arch. Int. Med. 103:783-790 (May) 1959 [Chicago].

Studies on cholesterol-fed rabbits in 2 laboratories have shown that nicotinic acid not only reduced serum cholesterol levels but resulted in partial (and often striking) protection against atherosclerotic lesions of the aorta. Conclusions drawn from these studies, though, cannot be transferred to humans. The use of large doses of nicotinic acid must be evaluated by controlled studies over many years before its effect on human atherosclerosis and its complications will be known. Such studies are in progress at the authors' clinic and elsewhere. Excluding those still in the first 24 weeks of therapy, the authors present their experience with 44 patients studied for periods of up to 2 years. Only the data from the first 56 weeks of treatment were considered in this report.

It was found that serum cholesterol levels can be reduced in the majority of hypercholesteremic patients by administration of large doses of nicotinic acid while the patients continue to eat their usual diets. The reduction is most prominent in the beta-lipoprotein cholesterol fraction, with reduction of the beta/alpha$_1$-lipoprotein cholesterol ratio. Nicotinamide is ineffective in reducing serum cholesterol levels. The only significant side-effects after ingestion of nicotinic acid are flushing and pruritus, which subside rapidly in the early stages of therapy and have not interfered with therapy. No toxic reactions have been found by clinical and laboratory observations, including a battery of 7 tests of hepatic function and needle biopsies of the liver in 17 patients after one year of therapy. Study for a much longer period will be required to determine

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The place of publication of the periodicals appears in brackets preceding each abstract.

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whether this form of therapy for hypercholesteremia will prevent or retard the progression of atherosclerosis in humans as it does in cholesterol-fed rabbits.

Interest and Importance of the Laboratory in the Management of Streptococcic Endocarditis. R. Martin, Y. Chabbert, B. Sureau and L. Martin. Presse méd. 67:667-670 (April 4) 1959 (In French) [Paris].

Various streptococci are capable of causing subacute bacterial endocarditis. Even those streptococci which are considered to be common and nonpathogenic saprophytes can be agents of this infection. The study of the bacteriostatic power with the classic antibiogram often results in the prescription of an antibiotic which is not the best choice. Therefore, it is necessary to interpret laboratory results and to ask for a quantitative study of the bacteriostatic power in liquid medium. Study of the bactericidal power of an antibiotic, or antibiotics in combination, is of great importance for the management of treatment and for prognosis. Penicillin and streptomycin are the antibiotics with the greatest bactericidal power. The penicillin-streptomycin combination is generally recommended for treating patients with group D streptococcic endocarditis. Penicillin alone is often sufficient in treating the form due to alpha-hemolytic streptococci. If the bactericidal action of the antibiotic, or antibiotics' combination, leaves a 1/1,000 survival of micro-organisms, therapeutic failure is possible; on the contrary, a rate of survival of 1/10,000 is favorable.

The "cellophane transfer" technique for the determination of the bactericidal power of antibiotics has the advantage of permitting photographic records which may be preserved and compared in case of variations in strain behavior. When endocarditis fails to respond well to treatment, a determination of antibiotic action may be performed on the patient's blood. Agreement between laboratory data and therapeutic results is obvious, as may be seen from the authors' statistics concerning 81 cases of streptococcic endocarditis. In 70% of the cases there was complete parallelism between the laboratory and the clinical course; 12% of the cases were not in agreement, and 18% were difficult to interpret.

Serum Transaminase in Diagnosis and Prognosis of Myocardial Infarction. K. Bobek, V. Karliček and V. Lahn. Ztschr. ges. inn. Med. 14:327-331 (April 1) 1959 (In German) [Leipzig, Germany].

The authors report on 70 men and 30 women, between the ages of 34 and 83 years, who were admitted to the medical clinic of the University in Plzeň, Czechoslovakia, for sudden pain in the chest or epigastrium. Immediately on admission blood specimens were obtained from these patients, and serial estimations of the concentration of serum glutamic oxalacetic transaminase (SGO-T) and serum glutamic pyroracemic acid (SGP-T) were made with the aid of the colorimetric technique at least once, but occasionally several times, daily for 3 consecutive days. In 41 of the 100 patients, the electrocardiogram showed myocardial infarction; the clinical picture and such laboratory findings as increased erythrocyte sedimentation rate, leukocytosis, and shortening of the coagulation column suggested myocardial infarction in 13; 26 patients had angina pectoris without signs of myocardial infarction; and in the remaining 20 other causes of the attack of pain, such as pulmonary embolism, bronchial pneumonia, rheumatic carditis, and necrosis of the pancreas, were observed.

Of the 54 patients with acute myocardial infarction, the transaminase activity was determined in 51 in time, and in all of these a significantly increased concentration of the SGO-T by 205 units, on the average, was noted. The serum transaminase values of the patients with angina pectoris were normal. A rise in the SGO-T level also was observed in the patients with pulmonary infarction, rheumatic carditis, and acute necrosis of the pancreas. Three of 9 patients with myocardial infarction, in whom the rise in the SGO-T level exceeded 300 units, died, and 4 had a severe course. The course of myocardial infarction was milder in 27 patients in whom the SGO-T activity varied between 100 and 300 units, and only one of these patients died. None of 15 patients with a SGO-T activity of less than 100 units died, and all of them had a mild course.

Serum glutamic oxalacetic transaminase estimations have a definite place in the diagnosis of myocardial infarction. A sudden rise and drop in the SGO-T activity favors with high probability the presence of myocardial infarction. Normal findings at the critical time are, with even greater probability, suggestive of the absence of myocardial infarction. The rise in the SGO-T activity and its duration also permit conclusions concerning the approximate extent of the necrosis and are, with the aid of other findings, of prognostic value.

Familial Cardiomegaly. G. Faive, J. Gilgenkrantz and J. Panthu. Presse méd. 67:673-676 (April 4) 1959 (In French) [Paris].

Familial cardiac hypertrophy, a recently described condition, is characterized by the presence of an enlarged heart, with no defined etiology, in a certain number of members of the same family. The authors examined 9 members of a family and found 3 cases in which there were electrocardiographic changes typical of hypertrophy and left ventricular overload with or without ischemic lesions. In the same family there were 2 cases of isolated enlargement of the heart without electrocardiographic alterations. No infectious or metabolic etiology was detected in 2 members even by means of intracardiac catheterization.

The disease is usually discovered between the ages of 20 and 25 years. There is no functional symptomatology in more than one-third of the cases; the minor symptomatology in the remaining two-thirds is characterized by effort dyspnea, rhythmic disturbance, lipothymia, or even syncope, frequently appearing rather late in the course of the disease. In more than one-half of the cases objective signs are in the form of a systolic murmur on auscultation. Radiologic examination is most important. Cardiac hypertrophy is global in about half of the cases, and left ventricular in the other half. A certain number of alterations reappear frequently in the electrocardiogram, giving a "family style" to all recordings. These alterations consist of changes in the ventricular complex and in the repolarization phase and of rhythm disturbances. Progress of the disease is considered less severe than formerly.

It is not known whether cardiac hypertrophy is an isolated form of a muscular or general metabolic illness or whether only the cardiac muscle is affected. It is likely to be hereditary. It is necessary to carry out a systematic familial inquiry when a primary enlarged heart is detected in a young subject.

Primary Hyperparathyroidism. J. Hellström. Nord. med. 61:551-556 (April 9) 1959 (In Swedish) [Stockholm].

The pathological changes in primary hyperparathyroidism consist of either adenomatous enlargement of usually one parathyroid gland or a so-called hyperplasia of all the glands. The cause is not certain. While the disease is relatively rare, the author's material was comprised of 112 cases, studied from 1930 to 1957 in patients aged from 16 to 71 years; 80% of the patients were women. Symptoms were often present for a long time before diagnosis was made. Calcification or stones in the kidneys were the commonest symptoms. Renal changes, alone or together with skeletal changes, were seen in 85% of the cases. Renal injury was present in all the cases of hyperparathyroidism, and there was more or less marked impairment in the concentration ability of the kidneys. A normal concentration test almost surely excluded hyperparathyroidism. In early cases the inability to excrete concentrated urine was of functional nature and could disappear after a successful parathyroidectomy. Hypertension, regarded as secondary to the renal changes, occurred in 70% of the cases. In earlier cases the hypertension was moderate and variable; later it became marked. In several cases it caused death or incapacity because of cerebral complications. The most typical skeletal change in hyperparathyroidism was osteitis fibrosa generalisata, considered pathognomonic for hyperparathyroidism. Marked osteitis was seldom seen. The skeletal changes always healed functionally if not anatomically. In 8 cases the first symptom of the disease was a giant-cell tumor in the upper or lower jaw. Gastroduodenal ulcer occurred in 33% of the male patients and in 3% of the female patients.

Diagnosis depends on clinical symptoms and on roentgenologic and laboratory examinations. The prognosis in untreated hyperparathyroidism is unfavorable. There may be so-called acute hyperparathyroidism with foudroyant course, or the course may extend over a long period, with recurring kidney stone and infection of the urinary tract. Spontaneous remissions occur, but certain recovery is unknown. The only rational treatment is excision of the hyperfunctioning parathyroid tissue. Internal treatment can be only symptomatic, and roentgen-ray treatment has been without avail. Operation may be simple when there is a solitary adenoma in the usual location; otherwise, it is difficult. In 22% of the cases reviewed, operation was unsuccessful or incomplete because of abnormal location of the adenoma, adenoma so small as to escape notice, or confusion with lymph glands or thyroid adenoma. Special difficulties are met with in primary hyperplasia, where all the parathyroid glands must be removed and only enough parathyroid tissue left to prevent insufficiency. The prognosis after parathyroidectomy depends on the degree of renal damage at the time of operation. Treatment should be centralized in hospitals equipped with the best facilities for scientific examinations, and operations should be performed only by surgeons experienced in thyroidectomy.

Antistreptolysin Titration in Certain Varieties of Glomerulonephritis: The Clinical Value of the Antistreptolysin O Titer. V. Scaffidi and A. Janni. Minerva med. 50:673-678 (March 7) 1959 (In Italian) [Turin, Italy].

The serum antistreptolysin O titer was measured in 31 patients with the following varieties of glomerulonephritis: diffuse acute or subacute variety (4 patients), localized acute or subacute variety (3), localized variety with tendency of the symptoms to recur and to become chronic (2), localized asymptomatic glomerulonephritis with tendency to become chronic (2), development of proteinuria after nephrotic or tonsillar syndromes (4), chronic glomerulonephritis associated with renal insufficiency (6), and other kidney diseases (10). Among the patients with the diffuse acute or subacute variety of glomerulonephritis, normal concentration of serum antistreptolysin O was observed in those instances in which the presence of hemolytic streptococci could not be established, and high concentration was observed with the presence of hemolytic streptococci. The hemolytic streptococcic origin of glomerulonephritis was also established in patients with the localized acute or subacute variety of the disease, although the serum antistreptolysin O titer was not so marked as in patients with the diffuse variety of the disease. There seemed to exist a certain correlation between the clinical course of glomerulonephritis and the antistreptolysin O titer. The titers returned within normal limits in patients in whom remission of the disease was rapid and complete. They persisted to be high, after remission of the acute phase of the disease of streptococcic origin, in those in whom the symptoms tended to become chronic. The values returned within normal limits only after complete remission of the disease took place. The titers were normal or were slightly elevated in patients with the chronic phase of the disease associated with renal insufficiency. This study suggests a close watch of patients who have had glomerulonephritis and in whom the antistreptolysin O titer persists to be high. The observance should last until there is complete normalization of the antistreptolysin O titer.

Facial Actinomycosis Misdiagnosed as Tetanus. J. Graham, K. Malmberg, R. Patey and A. Rubenstein. Illinois M. J. 115:271-273 (May) 1959 [Chicago].

In the 33-year-old man whose history is presented, the jaw muscles stiffened gradually until he was barely able to open his mouth. Four and one-half weeks previously he had "mashed" his left index finger on a grinding wheel, for which he had been treated and given a "tetanus shot." His canine teeth could not be opened more than three-eighths of an inch, and there was tenderness over the left masseter muscle. The left index finger was swollen, red, and tender, and there was a subungual hematoma. The patient was hospitalized, and the nail of the injured index finger was removed, and the area débrided. Cultures taken did not yield Clostridium tetani, but the patient was given 100,000 units of tetanus antitoxin and 1.2 million units of penicillin daily. Motion of the jaw improved, and he was discharged 5 days later.

Ten months later, in August, 1957, the patient's jaw again became tight. Examination now revealed a localized enlargement on the masseter muscle. The patient was treated with corticotropin and muscle relaxants for 4 weeks, but there was no improvement. The palpable mass was explored; the masseter muscle was split in the direction of its fibers. When the fascia was split, an encapsulated area of necrotic debris was found, which was removed by a curet. The area was drained, and nystatin (Mycostatin) powder was instilled. The debris contained a 3-mm. mass which was hard and yellow. The pathological report confirmed the suspicion of actinomycosis, as did the culture of the material. The patient was treated in hospital, with daily doses of 1,000 units of Mycostatin, 1.2 million units of penicillin, 1 Gm. of Chloromycetin, and a saturated solution of potassium iodide. The patient was discharged after one week, but daily injections of 1.2 million units of penicillin were continued for several months. Nine months later there had been no further recurrence of actinomycotic activity.

In retrospect, the authors say that the patient did not have the typical picture of tetanus; but when they were faced with the combination of a crushing, infected wound of the finger associated with trismus, and no other apparent cause for trismus, tetanus was considered. The possibility of actinomycosis should be kept in mind in obscure conditions around the cervicofacial area, particularly when a mass or infiltration is palpable. Treatment with penicillin or other antibiotic, combined with surgical excision, should be vigorous.

Nocardia Asteroides Infection: A Report of 7 Cases. M. C. Larsen, H. D. Diamond and H. S. Collins. A. M. A. Arch. Int. Med. 103:712-725 (May) 1959 [Chicago].

Nocardiosis is a granulomatous and suppurative infectious disease caused by the aerobic actinomycete, Nocardia asteroides. The authors report 7 new cases of this infection, the patients being treated at the Memorial Center for Cancer and Allied Diseases, New York, between 1952 and 1957. Attention is called to the presence of neoplastic disease in 5 of the 7 patients. The first case was of interest because the lesion was in an anatomic site previously unreported—the breast—and because of the likelihood that infection was exogenously introduced by a rose-thorn abrasion. Surgical extirpation, not antibiotic therapy, was credited with the cure in this case. The second patient was admitted because of chronic cough productive of thick, yellow, blood-streaked sputum. These symptoms were the residua of a severe pneumonia treated 5 weeks previously. Bronchoscopy revealed neither malignant cells nor tubercle bacilli. A large cystic cavity was observed 3 months later in the lobectomy specimen, and a sputum sample, obtained just before the operation, grew N. asteroides. The pathologist then restained the tissue sections with a modified Gram technique. Inspection showed gram-positive branching forms compatible with actinomycetes in the borders of the pulmonary abscesses and invading the lung parenchyma, thus establishing that Nocardia organisms played at least a partial role in causing the destructive lesions.

In the third patient, autopsy disclosed leukemic infiltrates in various organs; the presence of a grayish-yellow subpleural abscess in the right middle lobe of the lung was of special interest. A smear showed beaded, filamentous, long rods, some of which branched; on culture these were identified as N. asteroides. The fourth patient had chronic myelogenous leukemia; N. asteroides was isolated from 2 of 3 blood cultures during his last week of life. The fifth patient had been observed and treated throughout a 12-year period after radical mastectomy for carcinoma of the breast. Six months prior to death, hypophysectomy was performed to arrest metastatic disease. Twelve days before death deterioration began, with chills, myalgia, nausea and vomiting, lethargy, giddiness, and a sensation of retro-orbital fulness. At post mortem no tumor metastases were found in the brain, but a multiloculated abscess cavity contained greenish purulent material, which yielded N. asteroides in pure culture.

In the sixth patient, a man with chronic lymphatic leukemia of 4 years' known duration, a lung abscess developed. This was a remarkable instance of infection due jointly to Nocardia organisms and Diplococcus pneumoniae. Despite the persistent sensitivity of the Nocardia to chlortetracycline in vitro, and the disappearance of the organisms from the sputum during treatment with this agent, subsequent examination of the lung demonstrated that the infection had not been eradicated. The nocardial infection was cured by surgical extirpation and not by antimicrobial therapy. The seventh patient was a woman treated for generalized Hodgkin's disease over a 13-year period. Autopsy revealed numerous nodules in the lungs with central necrosis due to Nocardia. Similar lesions were found in the liver, pancreas, kidneys, and brain; cultures yielded N. asteroides. Surgical extirpation of the nocardial lesion produced cure in 3 instances. Death was considered due primarily to nocardiosis in 2 patients and to cancer in 2 others. Antibiotic therapy alone was not successful in eradicating the infection. The literature now suggests that sulfonamides might have proved more effective.

The Effects of Vitamin D and Gluten-Free Diet in Idiopathic Steatorrhoea. J. R. Nassim, P. D. Saville, P. B. Cook and L. Mulligan. Quart. J. Med. 28:141-162 (April) 1959 [London].

The treatment of celiac disease in children has been revolutionized since the observation of Dicke in 1950 demonstrated that the condition improved when the flour of wheat and rye was excluded from the diet. It was also shown that on this regimen fecal fat was reduced, and that the harmful effects of the flour were due not to the starch but to the protein (gluten) fraction. Later gluten-free diets were also tested in adults with idiopathic steatorrhea or with tropical sprue. It appeared that, whereas in infants and children the response to a gluten-free diet is universally good, only a proportion of adults may expect to be improved. With regard to the calcium balance in steatorrhea and the response to vitamin D, opinion is still not crystallized. The present paper concerns metabolic studies conducted in an attempt to provide further information concerning the actions of vitamin D and its relationship to gluten.

A consecutive series of 9 patients (2 male and 7 female) were studied. Their ages ranged from 8 to 60 years. All the patients were admitted to the metabolic unit of the Royal National Orthopedic Hospital in London. They were not confined to bed. In order to reduce the tedium of the diet, 3 daily menus were prepared and given in constant order of rotation. All the food was weighed, and the calculated daily values for calcium, phosphorus, nitrogen, and fat were made virtually identical in the 3 menus. The gluten-free diet produced clinical improvement in all the patients. The discontinuation of a gluten-free diet was usually followed by a violent clinical and biochemical relapse. The patients appeared to be very resistant to the action of vitamin D given orally or parenterally. There was evidence of increased sensitivity to the action of vitamin D when it was accompanied by a gluten-free diet, irrespective of the state of fat absorption. The level of serum inorganic phosphorus tended to be low before treatment, and 6 patients showed a definite increase in serum inorganic phosphorus after treatment with gluten-free diet or vitamin D. The calcium balance was studied in 7 patients. Four were in positive balance before treatment was begun. The calcium balance seemed to bear no relation to the degree of steatorrhea. Osteomalacia (pseudofractures or active rickets) was present in 5 patients; 3 of these patients had strongly positive calcium balances. A negative calcium balance was present in one patient without evidence of osteomalacia.

No consistent relationship could be demonstrated between the degree of steatorrhea and calcium absorption. All the patients who had good calcium absorption at the time of study had active osteomalacia. It is suggested that such patients pass through phases of positive and negative calcium balance, and that this phasic variation is not related to the degree of steatorrhea, but may be related to the degree of parathyroid activity. A marked increase in serum inorganic phosphorus followed treatment in 6 cases. It is suggested that this increase is a manifestation of parathyroid inhibition. The hypothesis that malabsorption of calcium in gluten enteropathy is due to a primary absorption defect was not supported by the data presented. Though there may well be such a defect, there is also a defect of intermediary metabolism involving vitamin D. Although the response to a gluten-free diet was favorable in every case, reversion to a normal diet resulted in a relapse to a degree of steatorrhea more severe than the original untreated condition. The advice to patients to take a gluten-free diet must, therefore, be tempered by the possibility that they may be worse if they are unable to maintain it.

Whipple's Disease: The Clinical Aspects. P. Farnan. Quart. J. Med. 28:163-182 (April) 1959 [London].

Whipple described the first case of the disease now referred to as intestinal lipodystrophy at Johns Hopkins Hospital in 1907. Farnan states that, of the total of 46 cases reported from America, 28 have been observed since 1950. He discusses the clinical aspects of the disease on the basis of 7 cases of intestinal lipodystrophy observed in Britain and of 60 other well-documented cases. The disease occurred predominantly in men (55 of 67 patients) of an average age of 43 years. The clinical pattern may be divided into a prodromal period, characterized by exacerbation of illness, and a final period of relatively rapid decline. Six features, all of them intermittent, are observed during the prodromal phase: arthritis, abdominal symptoms, diarrhea, cough, loss of weight, and asthenia. The prodromal phase in the 7 cases presented ranged from 2 or 3 years to 23 years, whereas the final period of decline lasted from 3 to 18 months. The disease may be more common than is suspected, and should be included in the differential diagnosis of the steatorrheas and chronic diarrheas.

The fully developed picture often suggests Addison's disease, but the absence of electrolyte disturbances should allow intestinal lipodystrophy to be considered. The main physical signs are usually found on abdominal examination. The triad of distention, upper abdominal mass, and radiologic evidence of gastric or duodenal displacement, or any 2 of these features, may be of help in diagnosis. Supporting evidence may be available in the cardiovascular or respiratory system. The results of laboratory investigations parallel those found in idiopathic steatorrhea; but the invariable presence of a normochromic or hypochromic anemia, the finding of occult blood in the stools, and the common association of gastric achlorhydria may help to differentiate the conditions. The diagnosis must be confirmed by the demonstration of the characteristic Schiff-positive macrophages. This may often require biopsy of the mesenteric lymph nodes, but the macrophages have also been demonstrated in the peripheral lymph nodes, and lymphadenopathy with an indefinite "sarcoid-like" picture should stimulate biopsy studies on lymph nodes. The basic lesion appears to be an alteration in the ground substance of the mucosa of the jejunum. Its periodic formation and dissemination may account for the protean symptoms of the prodromal period and for the extensive lesions found at autopsy; later, when produced in excess, it appears to cause obstruction of the lacteals at the mucosal site and the clinical features of a general malabsorption defect.

Until the advent of steroid therapy little could be done for these patients. The results of steroid therapy are capricious, but remission of some degree appears to be the rule, though eventually it is followed by relapse and death. There are no grounds for assuming a pituitary-adrenal mechanism to explain the main features of the condition. The demonstration by Black-Schaffer in 1949 of a mucopolysaccharide complex in the macrophages in the jejunum caused a reorientation of etiological concepts, and it now appears likely that the jejunal mucosa represents the source of the process.

Adult Leukaemia: Trends in Mortality in Relation to Aetiology. W. M. C. Brown and R. Doll. Brit. M. J. 1:1063-1069 (April 25) 1959 [London].

The deaths from leukemia which occurred in England and Wales for the period from 1945 to 1957 have been classified under 3 headings: (1) acute leukemias of all types; (2) chronic myeloid leukemia; and (3) chronic lymphatic leukemia. The age-specific mortality rates have been calculated for each type of leukemia, for each sex, and for 3 periods of time—1945-1949, 1950-1954, and 1955-1957. The data have been gathered for persons aged 15 years and over. Deaths attributed to plasma-cell leukemia have been excluded. It has been shown that, for each of the 3 periods studied and for each of the 3 different classes of leukemia, there was an appreciable increase in mortality with age during a large part of adult life. There was, however, an important difference in the trends of the mortality rates with time. Thus, in each age group the mortality from the acute leukemias increased between 1945 and 1957, whereas the mortality from the chronic leukemias, with the exception of chronic myeloid leukemia in men, increased during the period of observation only in the older age-groups. At these ages the mortality increased for all types of leukemia in both sexes, but the increase in chronic lymphatic leukemia in men was outstanding. The observed increase in the age-specific death rates of acute leukemia at ages under 60 years was largely real and due to increasing exposure of the population to leukemogenic factors in the environment, but most of the increase in the death rate from the chronic leukemias was due to their better recognition consequent upon improved medical care for the elderly.

The extent to which exposure to ionizing radiation may be responsible for at least some of the recorded increase in leukemia mortality has been the subject of controversy. It is important to note the evidence that radiation exposure has been associated with an increase in the acute leukemias more often than with an increase in chronic myeloid leukemia, and not at all with an increase in chronic lymphatic leukemia. The extent to which the increases in the national mortality rate from acute leukemia may be related to increases in our artificial radiation background can be adequately assessed only with greater knowledge of the basic mechanisms of cancer induction and of the relationship between radiation dose and incidence.

Multiple Myeloma: Two Cases with Unusual Clinical Symptoms. E. A. Ramírez. Bol. Asoc. méd. Puerto Rico 51:1-11 (Jan.) 1959 (In English) [Santurce, P. R.].

Eleven patients with multiple myeloma were observed at the Faculty of Medicine of the University of Puerto Rico over a period of 12 years. Three of these patients showed no specific bone lesions roentgenologically; in 3 others the symptoms were not those of multiple myeloma; and 5 did not have Bence-Jones proteinuria. The cases of 2 men, 59 and 80 years old, are reported. The finding of Bence-Jones protein was not demonstrated in the urine of either patient. The younger patient complained of illness of 2 weeks' duration, consisting of respiratory disorders, profuse perspiration at night, and moderate fever. On hospitalization he was dyspneic and cyanotic and had moderate fever. A Bucky chest roentgenogram showed enlargement of the heart, left-sided pleurisy, and bone lesions of the myelomatous type on the lower ribs, the clavicles, and the scapulas. Fluid obtained by a pericardiocentesis was serohemorrhagic. A chest roentgenogram after the pericardiocentesis showed a parietal pericardial thickness of 4 mm. The cardiac pulsations were almost unnoticeable on fluoroscopy. The electrocardiogram showed changes characteristic of pericarditis. The treatment consisted of the administration of digitalis, diuretics, and urethan. There was a slow regression of the clinical symptoms. The cardiac pulsations observed on fluoroscopy improved. The patient was discharged in satisfactory condition 5 months after hospitalization. Recurrences appeared, however, at intervals of 3 months, showing constant progression of the disease which did not respond to urethan treatment, and the patient died a year and a half after the appearance of the first symptoms. Autopsy showed multiple myelomatous lesions of almost all the bones and severe myelomatous lesions of the pleura and the pericardium. There was no valvular disease, atherosclerosis of the coronary arteries, lesions of rheumatic fever, or tuberculosis of the lungs or the pericardium.

The older patient complained of a large tumor which appeared on the right side of the frontoparietal region 3 months before consultation. Needle aspiration biopsy of the tumor showed multiple myeloma. Myeloma cells were also found in the bone marrow. The roentgenogram of the skull showed a defect corresponding to the lesion and numerous small defects of multiple myeloma. The treatment consisted of the administration of urethan, up to a total dose of 44 Gm., within a period of 3 weeks. A sudden marked regression of the tumor occurred several days after withdrawal of the drug, and this regression lasted 6 months. Recurrences, followed by regression of the tumor under the effect of urethan therapy, occurred 4 times at short intervals. Each regression lasted 2 to 4 weeks after discontinuation of the treatment, the patient receiving a total dose of 191 Gm. of urethan. In contrast to the good clinical response to urethan, constant radiologic progression of the lesion was observed. The patient died 2½ years after the appearance of the first symptoms. No autopsy was permitted.

In the 2 cases reported, the advanced period of the illness was marked by the development of acute anemia, disturbances of the electrolytes, mental confusion, and hemorrhages. The author believes that cases of multiple myeloma exclusively located on the pleura and on the pericardium have not previously been reported in the literature, his being the first to be reported. He directs attention to the good, but transient, effects of urethan on the tumor in the second patient, this medicament causing regression of the tumor several times in the presence of progression of the disease.

Immediate and Late Results in Radiophosphorus Therapy of Erythremia. E. D. Duboviy and M. A. Yasinovsky. Klin. med. 37:30-37 (April) 1959 (In Russian) [Moscow].

The authors report on 53 patients with erythremia treated with radiophosphorus (P^{32}). Good results were obtained in 48 of the 53 patients. In the majority of the cases, most pronounced clinical and hematological effects were obtained 3 to 5 months after the course of treatment with P^{32}. Relapses took place in less than 2 years in most of the patients. Repeated institution of the treatment usually produced a good effect. In the majority of the patients remission lasted 2 or 3 years, and in some of them 4 or 5 years.

SURGERY

Surgical Considerations of Occlusive Disease of Innominate, Carotid, Subclavian, and Vertebral Arteries. M. E. DeBakey, E. S. Crawford, D. A. Cooley and G. C. Morris Jr. Ann. Surg. 149:690-710 (May) 1959 [Philadelphia].

The authors performed arteriographic studies on 174 patients with manifestations of arterial insufficiency of the cerebrum and upper extremities. These studies revealed the presence of extracranial arterial occlusion in 73 patients (42%), 63 of them being subjected to operation. In this latter group of patients a total of 115 extracranial lesions occurred; these were located in the internal carotid, vertebral, innominate, common carotid, and subclavian arteries, single lesions being present in 31 patients and multiple lesions in 32. Eighty-eight lesions were explored surgically, and 75 obstructive lesions, occurring in 53 patients, were found to be segmental in nature and amenable to restorative operation. The reported observations are concerned with these 53 patients. The remaining patients had extensive complete occlusion of the internal carotid or vertebral arteries, and in view of the duration of the occlusion the lesions were not considered operable.

The proximal forms of the disease were evident clinically by the manifestations of arterial insufficiency of the cerebrum and upper extremities. The distal occlusions were manifested by cerebral arterial insufficiency. Due to the limitations of accurate localization of the lesions on clinical grounds, all the patients were subjected to arteriographic studies. Lesions occurring in the great vessels arising from the aortic arch were operable regardless of the location and extent of the occlusion. Incomplete occlusions of the internal carotid and vertebral arteries were similarly amenable to operation. Complete occlusions of the latter vessels were rarely operable unless explored soon after onset of symptoms. Surgical treatment was directed toward restoration of normal circulation. To achieve this objective, 2 types of procedures were employed, namely, endarterectomy and end-to-side bypass graft. Endarterectomy was employed in the treatment of well-localized lesions, and the more extensive occlusions were bypassed by means of a suitable arterial substitute. Endarterectomy was performed on 37 lesions, and graft bypass was employed in the treatment of 38 lesions. A pulsatile circulation was restored in the treatment of 72 of these 75 lesions. Circulation was restored in all patients with lesions involving the great vessels arising from the aortic arch, in 97% of those with operable lesions of the internal carotid artery, and in 60% of those with occlusions of the vertebral artery.

Severe cerebral arterial insufficiency manifested by coma and paralysis was present before the operation in 3 patients, and although circulation was restored in one or more of the occluded vessels, death resulted from irreversible ischemic damage of the brain. Two patients died of myocardial infarction after the operation, and one died of hemorrhage. All the patients with lesions of the great vessels obtained complete relief from their symptoms, and most of those with lesions of the internal carotid and vertebral arteries were either relieved or improved. These patients have been followed for periods of up to 5 years, and the success achieved by the operation has been well maintained.

Surgical Treatment of Occlusive Disease of the Carotid Artery. H. T. Bahnson, F. C. Spencer and J. K. Quattlebaum Jr. Ann. Surg. 149:711-720 (May) 1959 [Philadelphia].

The authors report on 9 women and 13 men, between the ages of 22 and 78 years, who underwent surgical exploration for occlusive disease of the carotid arteries. The commonest site of the occlusive lesions was near the bifurcation of the common carotid artery, this site being present in 20 of the 22 patients. Partial obstruction was present in 13 and complete obstruction in 7 of the 20 patients with upper carotid obstruction. The origin of the innominate or the left common carotid artery from the aorta and the adjacent portions of the carotid or innominate arteries or the aorta were involved in the remaining 2 patients with lower carotid obstruction. Endarterectomy was the procedure of choice in treating the patients with upper carotid obstruction, and bypass or direct replacement therapy was the preferred method for obstruction near the origin of the vessels from the aorta. In the usual operation performed expeditiously, no measure to support the distal circulation is necessary during the required temporary carotid occlusion. When the obstruction is unusual or extensive, a temporary bypass may be used to allow a longer period of safe operative occlusion.

The observations made in treating these 22 patients justify the following conclusions. A remediable narrowing of the carotid arterial system may be present in patients who have sudden or episodic unilateral motor or sensory disturbances, syncope, ocular symptoms, or speech disorders. A single symptom complex does not exist. Unilateral blindness and contralateral hemiplegia, described formerly as a hallmark of carotid occlusion, are present in only a small number of patients. The variations in symptoms reflect variations in collateral circulation and involvement of other vessels and emphasize the need for carotid arteriography in evaluation of these patients. Such an obstruction must be sought at both the origin of the vessels from the aorta and the bifurcation of the common carotid artery in the neck. The most favorable cases are those in which there is a history of transient attacks of neurological symptoms without significant continuing neurological deficit and in which an area of localized obstruction can be revealed. When symptoms are continuous and the neurological deficit is marked, benefit from surgical treatment is less likely. Of the 13 patients with partial upper carotid obstruction, 1 obtained complete relief, 7 were improved, and 5 were therapeutic failures, 2 of them dying within 24 hours and 1 week, respectively, after the operation. Of the 7 patients with complete upper carotid obstruction, 2 died, and 5 were therapeutic failures. Complete occlusion of the internal carotid artery will rarely be treated successfully unless the occlusion is of very brief duration. The 2 patients with lower carotid obstruction made a complete recovery.

Surgery of Subpleural Blebs: Indications and Contraindications. F. Feraru and C. S. Morrow. Am. Rev. Tuberc. 79:577-590 (May) 1959 [New York].

The authors report on 7 men, between the ages of 22 and 68 years, 3 of whom were operated on for subpleural blebs, while 4 presented varied contraindications to surgical intervention. The patients were studied by determination of the vital capacity and maximal breathing capacity with the aid of a 9-liter Collin's respirometer, a modification of the Benedict-Roth metabolism apparatus. Bronchospirometry was performed with the aid of a flexible double-lumen catheter. All the patients considered for surgical intervention were studied by bronchoscopy and bronchography unless contraindicated by extreme pulmonary insufficiency. Angiocardiography, which was performed on one patient, revealed avascularity of the bullous area.

Operation was performed with the aid of endotracheal anesthesia in as simple a manner as possible to provide minimal risk. The pleural cavity was entered through the 4th intercostal space anteriorly. All large blebs were unroofed. The parietal pleura was rubbed lightly with dry gauze to provoke adhesive reaction. It is believed that the operation should be conservative of lung tissue. Only giant blebs are considered for removal. They must be big enough to cause demonstrable compression of adjacent lung tissue. The blebs must be the major factor in the altered respiratory efficiency. Coexistent diffuse emphysema may also be present but is probably part of the same process. Any other added pulmonary disease should raise doubt of the primary importance of the blebs. Further studies, particularly of lung compliance, are indicated. The operation is recommended both as a prophylactic and as a therapeutic measure to improve pulmonary function.

A Case of Pericardial Cyst. G. Besa. Fracastoro 52:131-138 (March-April) 1959 (In Italian) [Verona, Italy].

The author reports on a 32-year-old man with a pericardial cyst which was treated surgically. A roentgenologic examination made when the patient was 24 years old showed a "double curve" of the left ventricle. Five years before operation he suffered occasional transitory pain in the precordium on exertion. Just prior to operation he had severe precardial pain radiating into the left shoulder, but these symptoms gradually disappeared in 3 days. Neither fever nor cough was present. A paracardiac shadow at the base of the left lung was noticed on roentgenologic examination of the thorax. The patient was subjected to posterolateral thoracotomy on the left, with partial resection of the 6th rib. An irregular oval swelling, the size of the head of a fully developed fetus, covered by the mediastinal pleura, was found adjacent to the pericardium. The anterior pole of the mass reached the anterior phrenicocostal angle. The diaphragmatic surface of the lower lobe of the lung adhered loosely to the parapericardial formation. After the lung had been completely freed and the phrenic nerve reflected, the mass was easily removed. The mass consisted of a voluminous grayish-yellow cyst, with thin, transparent walls, and was filled with fluid; a thin pedicle connected it with the pericardium. It was oval and had a translucid surface, measured 13 by 8 by 7 cm., and weighed 420 Gm. The author believes that the absence of clinical symptoms is not a necessary characteristic of a pericardial cyst and that the presence of clinical symptoms depends on the size and development of the neoformation.

An Analysis of Rupture of Thoracic Aneurysms Subsequent to Abdominal Aneurysmectomy. E. Senderoff, L. Blum and I. D. Baronofsky. Surg. Gynec. & Obst. 108:567-574 (May) 1959 [Chicago].

Although aneurysmal dilatation of the aorta is usually restricted to one particular location, the underlying pathological process of atherosclerosis, calcium deposition, loss of elasticity, and dilatation of the vessel wall occurs throughout the aorta, and in some cases multiple aneurysms are present. The authors present a clinical and pathological analysis of 2 cases of multiple aortic aneurysms. In both patients, men aged 55 and 72 years, respectively, the lowermost aneurysm was treated first, with fatal rupture of the most proximal aneurysm occurring relatively soon afterward. While one cannot definitely state that these events occurred as cause and effect, the supposition is a strong one.

In the surgical repair of abdominal aortic aneurysms, the aorta proximal to the aneurysm is completely occluded for a significant period of time. The authors cite studies carried out by others which showed that occlusion of the aorta in man affects the blood pressure proximal and distal to the point of occlusion. While the normal aorta with good elastic fibers in the media is able to withstand changes in blood pressure, the diseased aorta may not be able to withstand increased pressure. As seen in the cases presented, the thin walls of the thoracic aneurysms contain atheromatous plaques, areas of degeneration and necrosis, and fragmentation and depletion of the elastic fibers. If the increased intra-aortic blood pressure, resultant from aortic occlusion during surgical repair of the abdominal aneurysm, exerts a stress on the proximal vessel wall causing further fragmentation of the elastica, cracking of the atheromatous plaques, or beginning dissection of the necrotic wall, then the repair of the distal aneurysm may become an added factor in initiating the onset of the rupture of the proximal aneurysm. It is suggested that, in the event of staged repair of multiple aortic aneurysms, the most proximal aneurysm should be repaired first.

Rehabilitation and Work Capacity after Pulmonary Resection (Results 2 to 7 Years after the Operation in 291 Patients with Pulmonary Tuberculosis). F. W. Gierhake. Beitr. Klin. Tuberk. 120:135-149 (no. 2) 1959 (In German) [Berlin].

The author reports on 291 patients with pulmonary tuberculosis, who underwent pulmonary resection in the surgical clinic of the University of Giessen, Germany, between 1951 and 1955. Two to 7 years after the operation 252 (86.6%) of the 291 patients were living and were free of recurrence of tuberculosis. These 252 persons were examined concerning their work capacity. According to the findings, 215 (85.3%) were working; 23 (9.1%) were invalids, but they had a functionally satisfactory result and were able to do light work; 7 (2.8%) were still unemployed but were able to work; 3 (1.2%) were not able to work; and 4 (1.6%) were still being treated for postoperative complications. The reduced pulmonary function in the patients who did not work had already been essentially present before the pulmonary resection, or it depended on postoperative complications. A cause-and-effect relationship was present between these complications and the preceding collapse therapy and the long duration of the disease, but not between the postoperative complications and the resection. The rare recurrences, the slight operative risk in unfavorable cases, and the favorable functional results of pulmonary resection justify the recommendation to perform it on all patients in whom a cure cannot be obtained with conservative treatment and chemotherapy.

Carcinoma of the Stomach and Blood Group. H. W. Schreiber, W. M. Bartsch and W. Dauer. Beitr. klin. Chir. 198:193-205 (no. 2) 1959 (In German) [Munich, Germany].

The authors survey the literature concerning the correlation between blood group and disease. Whereas some investigators reported that patients with a certain blood group showed a greater tendency for such diseases as anemia, tuberculosis, diabetes, and various types of malignancies, others were unable to confirm these correlations. The authors had an opportunity to review the records of 311 patients with carcinoma of the stomach, who were treated at the surgical clinic of the University of Bonn during the decade from 1948 to 1957. These patients represented a selected group insofar as only those were included for whom the blood group was known and for whom the diagnosis had been histologically verified. The percental distribution of the blood groups of these patients and a comparison with the results on blood group distribution in gastric cancer obtained by another investigator are recorded in a table. The authors also present a critical analysis of the data on which the literature reports as well as their own studies are based. They conclude that there is no association between a certain blood group and carcinoma of the stomach, and that there is no proof of the so-called interior relationship between blood group and cancer of the stomach.

Hepatocerebral Intoxication as Complication After Portacaval Shunt Operation. J. Dortenmann and O. Müller. Beitr. klin. Chir. 198:206-214 (no. 2) 1959 (In German) [Munich, Germany].

The authors present the history of a 42-year-old man with hepatic cirrhosis, who 12 years before had undergone omentopexy because of severe ascites. After this operation ascites subsided, and the patient remained comparatively well until December, 1957, when he was again hospitalized because of the recurrence of ascites. After a severe hemorrhoidal hemorrhage, and because of a threat of bleeding from esophageal varices, a portacaval end-to-side anastomosis was made. Seven days after the operation the patient became comatose, and neurological examination revealed hyperreflexia of the right side of the body, a clonus of the right leg, an increase in tonus of the entire skeletal musculature, and compulsive gaze. Hepatic coma was thought of, but since fetor hepaticus, Kussmaul's air hunger, and increase in pulse frequency were absent, and since the neurological symptoms likewise did not fit in with the picture of hepatic coma, this diagnosis had to be rejected; hypokalemic coma could also be ruled out. The condition was diagnosed as hepatocerebral intoxication, in which loss of consciousness and clonic spasms are the chief symptoms.

The cerebral intoxication is caused by the absorption of ammonia (derived from the breakdown of proteins in the intestine) directly into the systemic circulation because of circumvention of the liver. Treatment consists in avoiding foods high in protein, particularly meats, and, in case of bleeding into the gastrointestinal tract (esophageal varices), stomach and intestine should be evacuated. The intestinal flora favoring protein decomposition should be suppressed in order to reduce the ammonia content of the blood. Observations suggest that the hepatocerebral intoxication is not so much a pathophysiological problem of the liver as it is the result of changes in the portacaval outflow system, and so the term "portacaval short-circuit syndrome" has been applied to it. Possibly the mode of anastomosis (end-to-side) is partly responsible, but this type of anastomosis has the advantage of being technically simpler and of being more secure against thrombotic occlusion than the side-to-side anastomosis.

PEDIATRICS

The Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery. J. D. Keith. Brit. Heart J. 21:149-161 (April) 1959 [London].

The author studied 10 children with anomalous origin of the left coronary artery from the pulmonary artery at the Hospital for Sick Children in Toronto. Fifty cases of this congenital heart defect were collected from the literature. In relating the condition to the child population in the Toronto Heart Registry, it appeared once among 300,000 children. This rare defect usually causes death within the first year of life, and at autopsy it is characterized by an enlarged, somewhat thin-walled left ventricle and a patchy fibrosis in the part of the left ventricle supplied by the anomalous coronary artery. The abnormal change would appear to be related more to the inadequate blood supply than to the oxygen content of the blood delivered. The diagnosis should be suspected in an infant in the first year of life in whom signs of heart failure develop, who has an enlarged heart, and from whom an electrocardiogram is obtained with evidence of myocardial fibrosis in the anterior portion of the left ventricle. The diagnosis may be largely confirmed by an aortogram carried out with the catheter just above the aortic valve. This will reveal filling of the right coronary artery from the aorta but will not reveal any filling of the left coronary artery. Adequate surgery has not yet been evolved, but it would appear possible that an anastomosis might be completed between a segment of the aorta at the site of the left coronary artery and a systemic artery. If this were carried out early enough before advanced myocardial change had occurred, normal heart function might result.

A New Simple Test Paper for Mass Detection of Phenylketonuria. J. Wortis and A. M. Giancotti. Am. J. Pub. Health 49:463-464 (April) 1959 [Albany, N. Y.].

Since phenylketonuria, a metabolic anomaly associated with mental retardation, can now often be beneficially treated with a phenylalanine-free diet, it has become desirable to detect its presence as early as possible, for the diet loses its efficacy as the child grows older. Test papers for the detection of phenylketonuria were developed by 2 pharmaceutical manufacturers. Small strips of the prepared paper are used by immersion in a fresh urine specimen or by simple pressure against a wet diaper. The studies reported were carried out with one of the test papers, in which the presence of phenylpyruvic acid in the urine produces a color change from the original yellowish white to a blue of varying density, depending on the amount of phenylpyruvic acid present.

The test paper was distributed by mail or handed to parents in a total of 1,600 families with retarded children. Six hundred of these children had been treated in the clinic, and 1,000 additional cases were contacted through the mailing lists of the New York Association for the Help of Retarded Children. The test paper was accompanied by an explanatory letter. This method of screening has provided fairly complete coverage for the children most likely to be helped; its chief advantage is that it can be carried out by technically untrained people at very little cost. The authors recommend that the test be widely used for similar surveys of large populations of retarded children. Since phenylketonuria may not be detectable during the first weeks of life, it should be adopted by pediatricians as a routine test for infants at least one month of age.

DERMATOLOGY

Alopecia Mucinosa. W. C. Johnson, R. S. Higdon and E. B. Helwig. A. M. A. Arch. Dermat. 79:395-406 (April) 1959 [Chicago].

Alopecia mucinosa is a dermatosis described by Pinkus in 1957. Clinically it appears as single or multiple, slightly erythematous, raised plaques, associated with loss of hair in the sites involved. Pathologically, the changes are in the pilosebaceous apparatus. After Pinkus presented his paper at the International Congress of Dermatology at Stockholm, Szodoray, of Budapest, said he had published a similar case with Lehner, in 1939, and he also referred to a case published by Kreibich, in 1926. Kreibich described a generalized patchy eruption in a youth, under the title "Mucin in a Skin Disease." The distinctive histopathological feature was the presence of cystic spaces and mucin within the pilosebaceous follicle. There was a perifollicular infiltrate with numerous lymphocytes and occasionally some mucinous material.

A review of cases previously diagnosed as alopecia, follicular hyperkeratosis, folliculitis, ichthyosis, keratosis pilaris, parapsoriasis, phrynoderma, and pityriasis rubra pilaris disclosed 8 examples of alopecia mucinosa at the Armed Forces Institute of Pathology. Of these, 1 case had previously been recorded as acute folliculitis; 2, as consistent with pityriasis rubra pilaris; and 5, as chronic folliculitis. Each of the 8 patients answered a questionnaire concerning the course of his disease and present status. The period of follow-up ranged from 3 to 13½ years from the date of onset. Paraffin-embedded tissue from the 8 patients was available for study and was examined with the aid of several staining and histochemical techniques. The histories of the patients are presented. The authors are of the opinion that the pathogenesis of alopecia mucinosa as a clinical and pathological entity is primarily a change in the epithelial cells within the pilosebaceous follicle, which results in the accumulation of mucin, inflammation in the corium being secondary. The mucinous material is an acid mucopolysaccharide and consists of hyaluronic acid or chondroitin sulfate or both. Pinkus suggested that the disease may be infectious, perhaps of viral etiology. The authors interpret the lack of evidence of contagion, the chronicity and recurrent nature of the eruption, and the histochemical similarity of the mucin to that seen in myxedema to indicate a metabolic process.

Idiopathic Lethal Granulomas of the Midline Facial **Tissues.** B. R. Alexander. A. M. A. Arch. Dermat. 79:390-394 (April) 1959 [Chicago].

The case of idiopathic lethal granuloma presented concerned a 48-year-old woman, in whom sprue had been diagnosed in April, 1956. When she returned in September, 1956, she complained of a sore throat, which had been treated unsuccessfully with penicillin and sulfonamides, of small painful nodules on her lower extremities, and of sinusitis and nasal "stuffiness" of several years' duration. The pharynx and soft palate were injected, and the tonsils were enlarged. There were tender, painful nodules on the lower extremities. Histopathological studies of tissue taken from one of these nodules showed changes consistent with periarteritis nodosa. The patient improved in the hospital without specific therapy and remained fairly well for a while. Six months later, though, she was readmitted with an ulcer at the junction of the soft and the hard palates of 8 weeks' duration. Roentgenograms of the hard palate showed a penetrating lesion into the floor of the right nostril. Fungous cultures from ulcer material were negative; bacterial cultures showed a mixture of Neisseria organisms and viridans streptococci. Histopathological studies showed necrotic granulation tissue.

In spite of broad-spectrum antibiotics and general supporting therapy, the ulcerative and necrotic lesion on the palate became more extensive and painful. A clinical diagnosis of idiopathic lethal granuloma of the midline facial tissues was now made, and the patient was given prednisolone. Within a week there was moderate improvement of the ulcer on the palate. Two weeks later swelling was noted on the right side of the nose and over the maxilla on the right. Transillumination revealed a shadow in the region of the right maxillary sinus, and it was assumed that the granulomatous process had extended. In spite of an increase in the dosage of prednisolone, the swelling progressed. There was loss of weight, weakness, cachexia, and progression of the granulomatous and ulcerative lesion. Terminally the patient's vision became blurred, the eyes bulged, the face was grossly deformed, and there was a serosanguineous discharge from the eyes and the nose. Death came 10 months after the onset of the pharyngitis.

The author reviews the literature and points out that malignant granulomas of the midline facial tissues are associated with chronic sinusitis, psychic trauma, upper respiratory infections, or sulfonamide therapy. It is hypothesized that subsequently a relative adrenal insufficiency develops and, because of a lack of the "antagonistic" effect of the adrenal cortical hormones, a local tissue allergy (Arthus' phenomenon) or periarteritis nodosa develops. The necrotic, ulcerative, and granulomatous processes follow. Because of the adrenal insufficiency, corticotropin (ACTH) and cortisone have been used for palliation. In spite of the patient's symptomatic improvement on these drugs, the malignant process continues, with a rather rapid termination of life.

The Relationship of Systemic Lupus Erythematosus and Discoid Lupus Erythematosus: A Clinical and Hematological Study. A. Scott and E. G. Rees. A. M. A. Arch. Dermat. 79:422-435 (April) 1959 [Chicago].

There are 2 main divisions of opinion with regard to the relation of discoid lupus erythematosus, originally described as a purely cutaneous disorder, to the systemic illness. While most clinicians feel that the 2 disorders are one and the same disease, merely representing the 2 extremes of one pathological process, there are a few dissenters who question this theory because of the large number of patients with cutaneous lesions who have been cured and have remained so without any evidence of involvement in other systems. The discussion received a fresh impetus by the demonstrations of Hargraves, Richmond, and Morton, in 1948, of the polymorphonuclear phagocyte with its basophilic inclusion body that has been given the name of "L. E. cell."

The authors present observations on 118 patients with lupus erythematosus, either systemic or discoid cutaneous, who have been clinically diagnosed as such and have been followed in St. Bartholomew's Hospital, London, during the past 8 years. These patients have been rechecked at least twice yearly on the basis of both clinical examination and laboratory investigation. The aim was (1) to classify these cases into groups on the basis of their clinical features, (2) to review these clinical features briefly, (3) to study the natural course of the disease in the several groups, (4) to consider the features which distinguish the cutaneous lesions of discoid lupus erythematosus from those observed in systemic lupus erythematosus, (5) to investigate the incidence of the L. E. phenomenon in the groups and to consider the value and import of this sign in the development and prognosis of the 2 diseases, and (6) on the basis of these studies to determine the relation between systemic and discoid lupus erythematosus.

One hundred two patients in this series had discoid lupus erythematosus. A grouping of these patients was made on the basis of clinical history, physical examination, and laboratory investigation. The L. E. phenomenon was studied in all of them as well as in a large control group. The results of the L. E. tests closely paralleled the clinical appraisal. By means of strict criteria for diagnosing systemic lupus erythematosus, the authors were able to make the diagnosis in only 12% of the patients with discoid lupus erythematosus. This proportion would be the maximum number, since inclusion of the total number of patients with discoid lupus erythematosus would reduce that percentage to 5%. No final conclusions could be made regarding the pathogenetic relationship of the 2 disorders.

Elastosis Perforans Serpiginosa: Elastoma Intrapapillare Perforans Verruciforme or Keratosis Follicularis Serpiginosa (Clinical and Histological Study of First Cases in the United States). J. M. Hitch and H. Z. Lund. A. M. A. Arch. Dermat. 79:407-421 (April) 1959 [Chicago].

The authors present the histories of 5 patients with elastosis perforans serpiginosa, which they believe to be the first cases of this skin lesion reported in the United States. They summarize salient features of 10 other cases observed in countries of Europe and Africa and reported under various names in the literature since 1945. All but 2 of the 15 patients were males. The lesions, usually on the sides of the neck, consisted of discrete papules which were firm, bright-red to saffron, with abrupt sides, and usually in an arciform arrangement. The papules had a keratotic cap which was firmly adherent and, on forceful dislodgment, left a bleeding crater. The skin of the central cleared region was hypopigmented, slightly rigid, and the site of prominent follicular orifices. Hair growth was not interrupted in either the active papules or the cleared central portion of the annular lesions. Specimens for histological examination were available.

The verrucous nature of the lesion is explained by marked acanthosis, with the formation of penetrating epidermal pegs and reactive proliferation of connective tissue in the papillary and subpapillary layers. The pathognomonic feature of the lesion is a peculiar proliferation of fibers resembling elastica. These often penetrate into the epithelium of rete ridges and the margins of follicles and sweat glands, and here and there open a channel to the cutaneous surface. The authors were unable to demonstrate intrafollicular penetration, but it is possible that sweat ducts are disrupted. The mechanism of penetration is not understood. It may be that the replacement of normal fine elastic fibers by the coarse and abnormal fibers around adnexal structures or at the dermoepidermal junction causes local physical changes leading to dermoepidermal separation or disruption of the margins of sweat ducts and hair follicles. The coarse fibers then penetrate the epithelium and lead to a reactive acanthosis. Perforation to the surface may be through the epidermal portion of the sweat ducts, but this has not been proved. Healing takes place by degeneration and phagocytosis of at least part of the proliferated elastic tissue, and there is a variable degree of ingrowth of fibrous tissue between the epidermis and the stratum reticularis. The fibrous tissue is largely collagenous, but interestingly it also contains some moderately fine elastic fibers.

The authors endorse the designation of "elastosis perforans serpiginosa," offered by Dammert and Putkoven, over those previously proposed by Lutz and Gruneberg, which they consider inaccurate. Though they are in general agreement with Miescher in regard to the histopathological picture, they find that the elastosis is not primarily or necessarily "intrapapillare," and surely it is not a tumor, as might be suggested by the suffix "oma."

OTOLARYNGOLOGY

Neomycin Ototoxicity. G. J. Greenwood. A. M. A. Arch. Otolaryng. 69:390-397 (April) 1959 [Chicago].

The author suggests some precautions in the systemic use of neomycin sulfate that may help to obviate ototoxicity. This report presents 20 cases of ototoxicity collected from the literature and an added case which corroborates the findings in the collected cases. To this end attention is directed to reports of the synergistic antibiotic-vitamin pharmacological action. Isotopically tagged chelated metals might be microradiographically utilized in an effort to uncover why specific drugs affinitively attack certain cellular constituents of the labyrinth.

The Ototoxicity of Kanamycin Sulfate in the Presence of Compromised Renal Function. R. F. Naunton and P. H. Ward. A. M. A. Arch. Otolaryng. 69:398-399 (April) 1959 [Chicago].

The authors report on 2 men, aged 40 and 48 years, in whom the hearing mechanism was severely damaged after the administration of relatively small doses of kanamycin sulfate (Kantrex). One of the 2 men had been given 14 Gm. over a 7-day period, and the other a total dosage of 5 Gm.

over a 5-day period. Each of the 2 patients had had a previous nephrectomy and was thus in a state of compromised renal function despite adequate urinary output. It is emphasized that new drugs with ototoxic potential should be used with the greatest caution, particularly in patients with questionable renal function.

Unusual Foreign Bodies in the Upper Respiratory Tract: Ten Cases of Leeches. C. A. Falidas. A. M. A. Arch. Otolaryng. 69:416-418 (April) 1959 [Chicago].

The leech is a very rare foreign body that can cause anxiety and other disturbances in the human host. The author reports 10 patients in whom leeches were found in the upper respiratory tract. These patients lived in a low land in the center of Greece where leeches are found in springs and brooks. During the summer season they, like others from their village, worked in the fields, where they used infested water. The entrance of a leech into the human system is often but a casual incident; however, early medical intervention is necessary to prevent a serious loss of blood and to spare the patient much anxiety. The construction of modern works for proper water supply can deliver a population from the threat of leeches. Appropriate education as regards the danger of drinking water without prior filtration may serve as a temporary preventive measure.

Bronchography in Carcinoma of the Lung. E. Huizinga. Pract. oto-rhino-laryng. 21:81-90 (March) 1959 (In English) [Basel, Switzerland].

The author studied 250 patients with carcinoma of the lung on whom bronchography was performed. In 179 of the 250 patients the bronchograms revealed an obstruction of a bronchus; in 33, a stenosis; in 4, a displacement of a bronchus; and in 1, a large cavity. Thirty-three bronchograms were negative. Although no abnormalities may be seen, the bronchograms are significant. The localization in a certain segment becomes clear, indicating in which bronchus Clerf's method of washing should be performed for the cytological examination. An anomaly in a large bronchus can easily be seen with the bronchoscope, but through bronchography more than one anomaly can be detected. In about 15% of the patients in this series bronchography revealed changes caused by metastases in the hilar glands, mostly stenosis of the main bronchus or of the lower part of the trachea, besides the anomaly of the primary tumor. These abnormalities are demonstrable by bronchoscopy and sectional radiography, but bronchography gives a better over-all picture.

Bronchography makes a "directed" bronchoscopy feasible. According to the indications obtained from the bronchogram, a certain branch is focused, and from this branch curetting is done blindly or a biopsy is performed with very fine forceps. Carcinoma of the lung nearly always arises from the mucosa of a larger bronchus. This is the reason why the obstruction of a certain bronchus is so often revealed by bronchography. However, the obstruction is often caused by pressure from the outside or by tissue in the lumen. Therefore, the bronchoscopist ought not to draw too far-reaching conclusions from the changes in the lumen seen with bronchoscopy. Sometimes a perfectly smooth surface in the bronchus is observed in cases of carcinoma as well as in cases of tuberculosis. An adenoma may be lobed, while with a common infection the mucous membrane may be granulated. Bronchograms performed on the 250 patients in this series revealed that the obstruction seen in 179 cases had a smooth outline in 99 and an irregular outline in 80, whereas the stenosis observed in 33 cases showed an irregular outline in 22 and a smooth outline in 11. In 36 patients the obstruction was located at the beginning of the bronchus and did not show on the bronchogram. In some cases the bronchus was missing on the bronchogram as the result of a compression, but often there were other causes. The completely smooth outline of the obstruction, plus the fact that the part of the lung concerned had diminished while other parts had increased in size, resulted in a picture which remained difficult to interpret. Clinical diagnosis on the basis of bronchograms should be established with the utmost consideration. Bronchography is a valuable contribution to bronchoscopy and lung surgery in that it enables disease conditions to be localized accurately, and indications regarding involvement of the main bronchi are obtained.

THERAPEUTICS

Crystalline Pancreatic Desoxyribonuclease as an Adjunct to the Treatment of Pneumococcal Meningitis. A. J. Johnson, J. H. Ayvazian and W. S. Tillett. New England J. Med. 260:893-900 (April 30) 1959 [Boston].

The authors report on 25 patients with bacteriologically proved pneumococcic meningitis, 19 (76%) of whom were either less than 4 months old or over 40 years of age, i. e., in age groups in which the prognosis of the disease is unfavorable, and 6 (24%) were between the ages of 4 months and 40 years. The patients were treated with massive doses of penicillin, given intravenously and intramuscularly, and ranging from 12 million to 40 million units per day. Six patients received 5,000 to 10,000 units of penicillin intrathecally on the first day. Crystalline pancreatic desoxyribonuclease was given intrathecally daily to each patient for 2 or 3 consecutive days in doses ranging from 50,000 to one million units per injection. Ten patients were near death on admission. Seven of these, and patients who were thought to have a cerebrospinal fluid block, were given intravenous and intramuscular injections of pancreatic desoxyribonuclease as well; one million units was given as a priming dose intravenously, and 2 million units intramuscularly at the same time. Twelve hours later, 2 million units was given intramuscularly. In this way a blood level of about 30 units was maintained during the entire 24-hour period. The intravenous and intramuscular injections were continued as long as seemed clinically desirable, but were rarely thought to be necessary for more than 2 or 3 days.

Three (12%) of the 25 patients died during the period of observation. Twenty-four (37.5%) of 64 patients with pneumococcic meningitis treated in a similar manner in the same hospital but without administration of pancreatic desoxyribonuclease died between 1951 and 1956. Severe neurological complications occurred in 1 patient, and mild complications in 2. Biochemical studies on the patients' cerebrospinal fluid showed that pancreatic desoxyribonuclease could be recovered from the spinal fluid in moderate amounts for 24 to 48 hours after a single intrathecal injection and that there was a transient increase in acid-soluble desoxyribonucleic acid and a striking decrease in desoxyribonucleoprotein in response to therapy with intrathecally administered pancreatic desoxyribonuclease. There was no evidence of local or systemic toxicity to crystalline pancreatic desoxyribonuclease during the course of this study.

Combination Phenylbutazone-Prednisone Treatment of Arthritis and Bronchial Asthma. M. Giordano, M. Ara and G. Tirri. Minerva med. 50:750-761 (March 14) 1959 (In Italian) [Turin, Italy].

A combined biochemical treatment with phenylbutazone and prednisone, consisting of the oral administration of tablets, each containing 50 mg. of phenylbutazone and 1.25 mg. of prednisone, was given to 73 patients with arthritis or bronchial asthma. The initial dosages varied but did not exceed 8 tablets a day; they were subsequently reduced to 6 or 4 tablets a day. Acute rheumatic disease was present in 18 patients, most of whom had a rheumatic carditis. The treatment produced improvement or disappearance of fever, improvement or complete subsidence of subjective symptoms after 5 to 10 days of treatment, amelioration of the cardiovascular state, and a tendency toward normalcy of the level of C-reactive protein, erythrocyte sedimentation rate, and antistreptolysin titer value. Prednisone alone was substituted for the combined therapy in 2 patients, which change was motivated more by investigative reasons than by the severity of the side-effects.

The combined treatment with phenylbutazone and prednisone produced a rapid regression of fever and joint pain and a fairly rapid disappearance of skin lesions in 2 patients with erythema nodosum. Primary chronic polyarthritis was present in 18 patients. Initial good response with the combined treatment was observed in 14 of these patients, which consisted in decrease of pain and swelling and improvement of articulation. Since only fair results were observed in the remaining 4 patients, prednisone alone, consisting of a daily dose of 25 mg., was subsequently substituted for the combined therapy; superior results with prednisone alone were obtained in one patient. Arthritis was present in 23 patients; the disease had multiple localization in 17 patients, and it was associated with diabetes mellitus in 8. The results of the combined therapy, except in patients with spondyloarthritis, were rapid and good. Patients with diabetes mellitus benefited from and tolerated well the combined therapy. The phenylbutazone-prednisone combination was also given to 12 patients with bronchial asthma; all these patients benefited from the treatment, but better results were observed in those with disease of recent rather than remote origin.

The greatest benefit of the combined treatment with phenylbutazone and prednisone in this series was derived by patients with arthritis. The combination exerted a synergistic action in the sense that relatively the same therapeutic effect in using the drugs singly could be obtained by using the combined preparation, the quantity of prednisone being reduced by one-half and that of phenylbutazone by one-third. This synergistic therapeutic action seemed not to be accompanied by a similar cumulative intensity of side-effects. Edema developed in the lower extremities in 2 patients but disappeared after treatment had been completed. Slight disorders of the gastrointestinal tract developed in 12 patients, compelling discontinuance of the treatment in one.

Abuse of and Dangers in Treatment with Antibiotics: Clinical Viewpoints. H. C. A. Lassen. Nord. med. 61:453-458 (March 19) 1959 (In Danish) [Stockholm].

The commonest mistakes in treatment with antibiotics are as follows: (1) treatment of fever where there is no diagnosis—antibiotics do not have an antipyretic effect; (2) wrong choice of antibiotics; (3) inadequate dosage, not infrequently with resulting masked effect, making exact diagnosis difficult; (4) overdosage and treatment continued too long with danger of toxic effects; (5) application in infections not influenced by antibiotic treatment; (6) inexpedient manner of administration; (7) failure to discontinue the treatment in the presence of complications; (8) failure to change the treatment in spite of the presence of mixed infection; and (9) application of prophylactic treatment except in a few justified cases. Caution in the use of antibiotics would undoubtedly do much to reduce the present-day excessive application and lessen the dangers in treatment with these substances which, rightly applied, are among the most important in the collective therapeutic armamentarium.

Abuse and Dangers in Antibiotic Treatment: Microbiological Viewpoints. H. Ericsson. Nord. med. 61:458-461 (March 19) 1959 (In Swedish) [Stockholm].

The microbiological dangers in antibiotic therapy are summarized as follows: Inadequate therapy becomes ineffective therapy. Antibiotic therapy becomes directly dangerous for the patient when attention is not paid to the action on micro-organisms other than the etiological ones and on parts of the body other than the affected milieu. Antibiotic therapy becomes dangerous for the patient's environment when applied so generally that it contributes to the origin and spread of nosocomial infections. Antibiotic therapy becomes dangerous for antibiotics in that it selects and favors relatively seen bacteria strains which are resistant. Only careful, rational employment of antibiotics can preserve the effectivity and safety of this important group of remedies for the individual patient and for the care of the sick on the whole.

Vitamin K Therapy in Liver Disease: Need for a Reevaluation. F. Steigmann, H. Schrifter, Z. D. Yiotsas and F. Pamukcu. Am. J. Gastroenterol. 31:369-375 (April) 1959 [New York].

The authors investigated the effects of large daily doses of vitamin K in patients with severe liver disease. In a group of 45 patients with cirrhosis, the average initial prothrombin concentration was 34% of normal. Twenty-four hours after the parenteral administration of 72 mg. of vitamin K, the average prothrombin concentration had risen to only 45%, and 48 hours later it had again dropped to 41%. In 22 patients, the hypoprothrombinemia was more marked 48 hours after than 24 hours after the administration of vitamin K. After a 48-hour determination had been made of the supply of prothrombin following the administration of 72 mg. of vitamin K, all the patients were given 50 mg. of vitamin K_1 (phytonadione) administered parenterally. The prothrombin concentration was again determined 24 and 48 hours later, when the average was found to be 49 and 50% respectively.

There are a number of reports in the literature in which excessive amounts of vitamin K have been found to increase the hypoprothrombinemia in patients with severe liver disease. The further depression of the prothrombin level in some patients after parenteral administration of vitamin K suggests that in these cases the liver appears to be functioning at its maximum capacity under the prevailing conditions. The depression may be the result of inadequate production of the substrate with which vitamin K combines, or of abnormal utilization of the substrate with consequent interference with prothrombin formation. The fact that in some patients with liver disease there is either no response or even no depression of the prothrombin level would speak for an exhaustion phenomenon in these particular instances. It has, therefore, been suggested that patients with liver disease and hypoprothrombinemia should be given a small dose of vitamin K and the dose should be repeated only if the prothrombin concentration does not show any further increase. The only manner in which the prothrombin activity can be increased in patients with hypoprothrombinemia who do not respond to vitamin K therapy is by means of transfusion, preferably of whole fresh blood or of frozen plasma.

The Treatment of Nonspecific Ulcerative Colitis by the Topical Administration of the Corticosteroids. M. Patterson and J. McGivney. Gastroenterology 36:480-486 (April) 1959 [Baltimore].

The fact that the corticosteroids have been found useful topically in inflammatory conditions of the skin, eyes, and joint cavities stimulated the authors to study their use in this manner in nonspecific ulcerative colitis. Twenty patients with nonspecific ulcerative colitis were treated. Stools were checked for pathogens, and barium enemas were given. Proctoscopic examinations were given prior to and at frequent intervals during treatment. In addition to the topical steroid therapy, all the patients received bland diets, antispasmodics, sedatives, antidiarrheal agents, blood, or antibiotics when indicated. When the response was good, treatment was continued for from 2 to 4 weeks. When no response was evident at the end of 2 weeks, therapy was discontinued, and if the proctoscopic picture showed exacerbation, therapy was discontinued at once.

The topical steroid therapy was given in 3 different forms: 1. Patients having acute or chronic ulcerative colitis limited to the rectum or rectosigmoid, and without systemic symptoms, were given suppositories containing 10 or 15 mg. of hydrocortisone acetate 3 times a day and at bedtime. It was found that, for optimal effect, the patient should defecate before insertion, so that the rectum would be empty. Women patients were encouraged to urinate before the suppository was inserted as the material was lost during urination. 2. Patients with more acute or chronic disease, who did not respond to suppositories or in whom the process was believed to extend higher into the colon, were given rectal instillations, twice a day, of 50 mg. of hydrocortisone acetate or 10 mg. of prednisone. The tablets were crushed and suspended in 100 ml. of water. The patient was advised to defecate or to flush the rectum with 3 oz. of warm water and to lie down for 30 minutes to an hour after the treatment in the morning and to reserve the evening treatment until bedtime. The instillations were to be self-administered by means of a 3-oz. syringe. 3. In patients in whom a larger area had to be treated, the therapy was given in the hospital once a day with a solution of hydrocortisone sodium succinate (100 or 200 mg.). This solution was added to a 250-ml. or 500-ml. bottle of isotonic sodium chloride solution, and the bottle was attached to an intravenous set. A plastic nasal catheter was then attached to the needle adapter, and the catheter was inserted into the rectum. The solution was started at 20 to 40 drops per minute, but the regulator clamp was so placed that the patient could increase or decrease the flow as long as the urge to defecate was not stimulated. In most patients, the proctoclysis was finished in 1 to 3 hours.

The best results were obtained in patients with early lesions and mild symptoms. The poorest results were observed in patients with long-standing and far-advanced changes, or in those who because of tenesmus or rectal disease could not retain the material. The 78% of over-all good results were no better than with many other forms of therapy in this disease. The impressive features of this therapy were the rapidity with which clinical and sigmoidoscopic remission was obtained, plus the added advantage of minimal absorption of the hormone.

Treatment of the Nephrotic Syndrome with Triamcinolone. L. Hellman, B. Zumoff, A. Minsky, N. Kretchmer and B. Kramer. Pediatrics 23:686-689 (April) 1959 [Springfield, Ill.].

In this report only acute remissions of the nephrotic syndrome after triamcinolone therapy are considered. No conclusions have been drawn regarding the effects of the treatment on the ultimate fate of the 15 children reported. The authors administered triamcinolone (Aristocort) to 4 girls, ranging in age from 1 to 9 years, and to 11 boys, ranging in age from 2 to 5 years, with the nephrotic syndrome. Two of the 15 children had hypertension; one of these had normal concentration of urea nitrogen in the blood and normal urea clearance, whereas the other had azotemia. The remaining 13 children had the nephrotic syndrome in its characteristic form, with all the typical clinical and laboratory findings, but without the stigmata of renal insufficiency. The duration of the nephrotic syndrome in these patients ranged from 15 days to 36 months. Twenty milligrams of triamcinolone was administered orally, in 5 daily doses of 4 mg. each, for 30 to 45 days.

Triamcinolone proved to be a highly effective therapeutic agent. Of the 15 patients treated, 10 had complete remissions and 4 had partial remissions. One of the latter children, who had hypertension without azotemia, received 2 complete courses of triamcinolone; the first course was a failure, but the second produced a partial remission. In another patient with hypertension and azotemia, the treatment was a failure and was discontinued. The typical response to treatment with triamcinolone was an abrupt diuresis, beginning 10 to 12 days after the initiation of treatment and resulting in the complete disappearance of retained fluid in the next 3 or 4 days. During the period of diuresis, the urinary excretion of protein decreased rapidly, and by the time diuresis was complete, the urinary findings were usually within normal limits.

The mere induction of acute remissions, no matter how readily or reproducibly, should not be the chief concern in the therapy of nephrosis. The ultimate prognosis is still pessimistic, despite regimens with currently available steroids. A recent report suggests that the long-term results of steroid therapy in the nephrotic syndrome might be improved by earlier, more intensive, and more prolonged treatment. The authors believe that triamcinolone is a useful steroid for such a program because of its high potency and minimal side-effects. The doses employed did not cause hypertension or retention of sodium.

PATHOLOGY

Capacity of Human Coronary Arteries: A Postmortem Study. F. L. Rodriguez and S. L. Robbins. Circulation 19:570-578 (April) 1959 [New York].

The authors studied the volume capacity of the coronary arteries of 100 hearts which were obtained at autopsy from 57 men and 43 women. Of the 100 hearts, 14 had myocardial infarcts, 7 had chronic valvular disease, 10 had miscellaneous forms of cardiac abnormality, such as bacterial and nonbacterial endocarditis and cardiac mural thrombosis not associated with valvular disease or myocardial infarction, and 69 were normal or had such abnormalities as cardiac hypertrophy and mild coronary or valvular atherosclerosis. The ages of the 100 persons varied from 13 to 95 years. Twenty-eight of them were emaciated, 18 were obese, and 54 were nutritionally normal at the time of death. The amount of Schlesinger's barium sulfate-gelatin injection mass entering the coronary arterial tree under standard conditions was taken as a measure of its capacity. The weight of the heart in the normal and disease state, the cross-sectional dimensions of the main coronary arteries near their origin, and the sex, age, and nutrition of the persons at the time of autopsy were analyzed.

The results showed that the capacity of the coronary arteries increased with the weight of the heart. The relationship between the capacity of the coronary arteries and the cardiac weight was not directly influenced by the presence or absence of cardiac abnormalities other than hypertrophy, or the sex, age, and nutritional status of the person. In persons with cardiac hypertrophy, the increase in the capacity of the coronary arteries did not keep pace with the cardiac mass. In hearts with normal coronary arteries, the capacity of the coronary arterial tree varied in direct proportion to the dimensions of the main coronary arteries near their origins. In hearts with severe coronary atherosclerosis, the over-all capacity of the coronary arterial tree may be maintained despite the diminution in size of its larger components. In hearts from emaciated subjects, the capacity of the coronary arteries was generally reduced in proportion to the loss in cardiac mass.

Primary Pulmonary Alveolar Carcinosis: Carcinoma: So-Called Pulmonary Adenomatosis or Alveolar-Cell Tumor: Review and 12 Personal Cases. E. Roelsen, T. Lund, T. Søndergaard, B. Møller and A. Myschetzky. Ugesk. laeger **121:** 397-407 (March 12) 1959 (In Danish) [Copenhagen].

Pulmonary cancer usually occurs as a primary bronchogenic tumor or as a metastatic process. A third tumor form, the so-called adenomatosis of the lung or alveolar-cell tumor, is a cancer which originates primarily in the lower respiratory tract. Pathologically it is a nosographic entity. Since the first case was reported by Malassez in 1876, more than 200 cases have been published. Presumably cases have been overlooked, both clinically and pathologically, or have been confused with pneumonia. Pulmonary adenomatosis occurs equally often in men and women. It is generally multiple and is localized to one or more lobes and frequently to both lungs. The nodes have a tendency to confluence, by which the diffuse form arises. There is no primary tumor in any other organ. The cases of 12 patients seen by the authors in the course of 8 years in a limited area in Denmark are tabulated; 2 representative cases are described in detail. Eight cases are typical of the diffuse primary pulmonary alveolar carcinosis; 4 cases represent the same histological cancer in its solitary form. The patients with the diffuse form were nonsmokers or nearly so; 3 of the 4 with the solitary form were heavy smokers.

Cough and expectoration are common symptoms for both the diffuse and the solitary forms of pulmonary adenomatosis; dyspnea and cyanosis dominate in the diffuse form. Cough, increasing as the processes progress, is the most conspicuous symptom. The most important criterion clinically is the roentgen-ray picture. The multiple or diffuse form is varied and is difficult to diagnose definitely; in the solitary form there is a solitary infiltrate or round shadow. Invasive growth in lymph tracts is common. The characteristic histological picture shows lung alveoli and alveolar ducts covered with a cylindrical or cubic epithelium which may take on an anaplastic, malignant character. The alveolar structure is preserved. Most important macroscopically are the changes, like those in gray hepatization, seen in cross section. In the series presented, the 8 patients with the multiple form of the disease died within 8 months after the onset of the symptoms. The other 4 patients were operated on, and 2 are living, 5 years and 16 months, respectively, after the operation.

Congenital Absence of the Parathyroid Glands. D. H. Lobdell. A. M. A. Arch. Path. 67:412-415 (April) 1959 [Chicago].

Reports of congenital absence of the parathyroids leading to infantile tetany and death are rare and until now have been confined to the European literature. The case described is that of a child who manifested a parathyroprivic picture throughout his 2 months of life. It is the 5th recorded example of congenital agenesis of the parathyroid glands. This full-term infant, weighing 2,920 Gm. (6½ lb.), was delivered spontaneously from a 24-year-old mother, whose prenatal course was complicated only by anemia. A sibling of the infant was in good health. Neuromuscular hyperirritability was noted at birth. At 39 hours the child was described as a normally developed but "very jumpy" boy, with jerky movements of the extremities when crying or disturbed. Deep tendon reflexes were hyperactive, and periodic clonus was noted. There was no carpopedal spasm or Trousseau's sign. The child had frequent episodes of tetany, manifested by generalized stiffness and shaking, slight cyanosis, and a high-pitched scream. Calcium chloride and calcium gluconate were administered per os, with poor response. Administration of the parathyroid hormone, parathormone, (Ellsworth-Howard test) resulted in more than a twofold increase in urinary phosphate excretion, excluding lack of kidney end-organ response to parathyroid secretion as an etiological factor. Addition of massive doses of vitamin D to the therapeutic regimen resulted in reversal of the abnormal calcium-phosphorus ratio. Oral administration of calcium was discontinued at one month of age, as the infant's neuromuscular hyperirritability diminished. Two tetanic seizures during the 5th week of life were controlled by calcium gluconate.

The child died when 55 days old, and the autopsy findings are described. The author feels that there is little doubt that this is a case of congenital absence of the parathyroid glands. Conditions which can lead to hypocalcemia and tetany, such as chronic intestinal dysfunction, renal insufficiency, and vitamin D deficiency, were not present. The 2-month duration of the symptoms is not compatible with ephemeral "tetany of the newborn." Step sections of the neck organs did not reveal parathyroid tissue. The thymus, which develops with the parathyroids from branchial pouches III and IV, was absent. In addition, 2 other congenital malformations, agenesis of the thyroid isthmus and an anomalous vascular ring, were found.

BOOK REVIEWS

Headache: Diagnosis and Treatment. By Arnold P. Friedman, M.D., Associate Professor of Neurology, Columbia University, New York, and H. Houston Merritt, M.D., Professor of Neurology, Columbia University. Cloth. $8. Pp. 401, with illustrations. F. A. Davis Company, 1914-16 Cherry St., Philadelphia 3, 1959.

This book is the product of 12 authors in various fields of medicine who have had wide experience in the diagnosis and treatment of patients with headache. Each author discusses the problem of headache from the standpoint of his specialty. There is some duplication in the text, for each author has been permitted to express his own viewpoint, but this seems to add to, rather than detract from, the volume. While the authors state in the preface that the book is written for the practicing physician, it is so comprehensive in its scope that physicians in all fields of medicine should find it interesting reading. Throughout the book, the basic mechanisms involved in the production of headache and head pain and the correction of these disturbances are stressed. The book has full chapters on mechanisms of headache; diagnostic principles and methods; principles of pharmacotherapy; the eyes, ears, nose, and throat as sources of headaches; migraine and tension headache; the role of allergy in headache; headache in systemic disease and in intracranial disorders; psychiatric and psychogenic factors in headache; the role of the cervical spine in headache and head pain; major cranial neuralgias; and the surgical treatment of headache. The chapter on principles of pharmacotherapy is especially good and should be of great interest to the general practitioner. Helpful therapeutic measures and prophylactic aids are adequately discussed. The approach to the headache problem is practical and, for the most part, thorough. Since temporal arteritis constitutes a medical emergency, more than the one and one-half pages allotted could have been devoted to the subject. Adequate references are given at the end of each chapter, and the book is well indexed.

The Upper Atmosphere. By H. S. W. Massey, Ph.D., D.Sc., F.R.S., and R. L. F. Boyd, Ph.D. Cloth. $17.50. Pp. 333, with illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1959.

This book is doubly interesting because of the spectacular successes of the recent International Geophysical Year and the increasing importance of aviation in medicine. After an introductory chapter on the necessary fundamentals of physics, there are chapters on the methods used for studying the upper atmosphere (balloons, rockets, sound waves, radio waves), on the ozonosphere and ionosphere, on lights in the night sky (especially the aurora borealis), on regular and irregular magnetic phenomena in the atmosphere, on meteors and cosmic rays, and on artificial satellites. Commendable features are the wealth of new and instructive material in the first chapter, the concreteness of detail in the chapters that follow, the abundance and beauty of the illustrations, and the generally direct and unaffected style. An almost negligible fault is the use of obsolescent units and symbols in the table describing the first six artificial satellites. The bibliography is good and the index excellent. Readers prepared to follow the occasional mathematics will find the equations explicit and accurate. Readers not so prepared must learn to skip the mathematics and enjoy the rest; the experience should be rewarding.

Psychopharmacology: Problems in Evaluation. Proceedings of conference on evaluation of pharmacotherapy in mental illness sponsored by National Institute of Mental Health, National Academy of Sciences—National Research Council, and American Psychiatric Association, Washington, D. C., September 18-22, 1956. Edited by Jonathan O. Cole and Ralph W. Gerard. Publication 583, National Academy of Sciences—National Research Council. Conference supported by grant no. 3M-9104 from National Institute of Mental Health of National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare. Cloth. $6.50. Pp. 662, with illustrations. National Academy of Sciences, National Research Council, 2101 Constitution Ave., Washington, D. C., 1959.

The six working papers which were prepared for the conference here reported reviewed, in a general way, the pharmacology of the drugs used in psychotherapy, effects on animal behavior, the reported results of clinical studies, their possible public health implications, and the more general problems of the evaluation of the effectiveness of any psychiatric therapy. The first section of the volume consists of these six working papers. Five committees were formed, composed mostly of members of the Committee on Preliminary Screening of Drugs, which thoroughly reviewed current knowledge of the basic mechanisms of action of these psychoactive compounds and, more particularly, the adequacy of available methods for the selection of the test animal and early human screening of compounds of this general sort. Three other committees were originally organized as a group, so that the field of clinical drug evaluation, which was the primary concern of

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

the conference, would receive the most thorough scrutiny possible. The general clinical area was divided into three sections. The first dealt with the problems attached to the selection of patient groups for study and the problem of adequate scientific controls in clinical researches. The second encompassed the influence of the environment in which the drug studies were done and the problems attached to drug administration itself. This area was expanded to include the more general aspects of test design in clinical drug evaluation. The third concerned itself with the problems of evaluation and the more detailed consideration of some of the available techniques for the measurement of change in psychiatric patients.

The committee on planning and coordination advised the National Institute of Mental Health about the formation of what is now called the Psychopharmacology Service Center. It had become increasingly apparent that there was serious need for a unit within the National Institute of Mental Health to concern itself specifically with the stimulation of research and the dissemination of information concerning the psychoactive drugs. This center was subsequently established with Dr. Jonathan Cole as its chief and Dr. Ralph Gerard as the chairman of its advisory committee. Because of the necessity for keeping this work from expanding into several volumes only that material which appeared to be most pertinent was included.

The summaries prepared by the various committees and presented to the main conference, together with discussion from the floor of these summaries, are included as a special section at the end of the volume and are followed by Dr. Seymour Kety's final analysis of the work of the conference and the consolidated recommendations of the various working groups. This volume contains the most valuable information on the evaluation of pharmacotherapy in mental illness that has ever been published. It is a storehouse of the current knowledge of this subject contributed by scientists who have engaged in research in this field. There is an author and discussant index, and a subject index.

A Textbook of Pharmacology and Therapeutics, Including Drugs and Solutions. By Harold N. Wright, M.S., Ph.D., Professor of Pharmacology, University of Minnesota, Minneapolis, and Mildred Montag, Ed.D., R.N., Professor of Nursing Education, Teachers College, Columbia University, New York. With appendix on Canadian drug legislation by Charles W. Nash, B.Sc., Ph.D., Professor of Pharmacology, Faculty of Medicine, University of Alberta, Edmonton, Canada. Seventh edition. Cloth. $5. Pp. 497, with 95 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

This new and extensively revised edition of an established textbook presents a wealth of up-to-date information about drugs and the newer, as well as the older, therapeutic agents in a concise and readable form. Students of nursing should find it an excellent introduction to pharmacology, and graduate nurses may find it useful as a brief reference work and a source of information about newer drugs.

The major portion of the text is devoted to a systematic review of the basic pharmacology, clinical uses, and toxicology of drugs currently employed in medical practice. A list of available preparations is given for each drug and conforms with the current editions of the U. S. P. and N. F., and the 1958 edition of New and Nonofficial Drugs. Doses are stated in both the metric and the apothecary systems, and both nonproprietary and trade names are included. A bibliography of relevant published papers is presented for each group of drugs.

There are also sections on phamaceutical preparations, techniques of administration of drugs, a review of arithmetic, a description of the elements and terminology of ward orders and prescriptions, a section on the emergency management of cases of poisoning, and a brief summary of drug legislation, both of the United States and of Canada. The material on the preparation and properties of solutions, a feature of earlier editions but more recently published separately, has been restored to the text.

The new format and typography are especially pleasing and contribute significantly to the clarity of the presentation. This is one of the better available pharmacology textbooks written specifically for nurses. Since the book is not directed to physicians and medical students, no criticism is implied in pointing out that these groups would probably find the book insufficiently detailed for their purposes.

Medical Department, United States Army, Surgeon in World War II. Volume II: General Surgery. Prepared under direction of Major General S. B. Hays, Surgeon General, United States Army. Editor in chief: Colonel John Boyd Coates, Jr. Editor for general surgery: Michael E. DeBakey, M.D. Associate editors: W. Philip Giddings, M.D., and Elizabeth M. McFetridge, M.A. Office of Surgeon General, Department of Army, Washington, D. C. Cloth. $4.25. Pp. 417, with 43 illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1955.

This volume comprises a clear and succinct account of the methods so successfully used by American Army surgeons in World War II. These methods represented a distinct advance over those used in World War I and resulted in a much lower death rate than had ever before been experienced among the wounded of any war.

One reason for the improvement was shortening the elapsed time between injury and operation. Previously the patients had been handled too much and transported too far and there were too many delays for inspection along the line of evacuation.

This was corrected by operating on all acute emergencies in the forward areas. Resuscitation was vastly improved, and it was learned early that plasma was not an adequate substitute for whole blood. The use of oxygen was highly important. Cyanosis could be easily overlooked in a hasty examination under a poor light in the preoperative tent. The importance of emptying the stomach preoperatively was recognized early. Abdominal surgery, which was largely neglected in World War I, made a great advance in World War II, principally due to early operation and to the invariable rule that all wounds of the large intestine should be exteriorized or, if that is not possible, must have a colostomy proximal to the wound. It was learned that methods involving suture and packing of liver wounds did not give good results but were followed by secondary hemorrhage, abscess formation, or liver necrosis. Most liver wounds stop bleeding spontaneously. Exploration and drainage of Morison's pouch to prevent biliary peritonitis was the method eventually evolved.

The transdiaphragmatic approach to thoracoabdominal wounds was another advance. It was also learned that too much morphine had been given previously. Repeated doses when a soldier was wet, chilled, and his circulation poor resulted in nonabsorption and subsequent poisoning when he was warmed up and resuscitated in the preoperative tent. This book makes a valuable contribution to the subject of traumatic surgery.

The Comparative Anatomy and Physiology of the Nose and Paranasal Sinuses. By Sir Victor Negus, D.Sc., M.S., F.R.C.S. Cloth. $14. Pp. 402, with 178 illustrations. [Williams & Wilkins Company, 428 E. Preston St., Baltimore 2]; E & S Livingstone, Ltd., 16 & 17 Teviot Pl., Edinburgh 1, Scotland, 1958.

In 1929 a monograph on the comparative anatomy and physiology of the larynx appeared. The anatomic and physiological investigations on which this monograph was based took seven or eight years and were made at various institutions, among them the Zoological Society, the Museum of the Royal College of Surgeons in London, and the laboratories of Kings College. This study on the mechanism of the larynx throughout the animal kingdom, its interrelation with olfaction, respiration, phonation, and possibly other functions, was painstakingly undertaken. All this, presumably in his spare time, was done by one whose chief interest was that of a practitioner and "student" of the ear, nose, and throat in health and disease. This monograph on the larynx at once became a classic and has so remained.

The collection in the Museum of the Royal College of Surgeons of England which illustrates the anatomy of the human nose and sinuses, and which was arranged about the famous aggregation of specimens of Professor Onodi of Budapest, was almost completely destroyed during the bombing of London in 1941. The author, prompted by the need for reconstruction of this collection and using the ample materials of the storerooms of the College of Surgeons, once more devoted the leisure time of several years to this task and, in addition, supplemented the human material with specimens from various animals, including fish, amphibia, reptiles, birds, and mammals.

The result of these labors is comparable to that first work on the larynx. This handsomely bound and printed volume, embellished with numerous illustrations, nearly all of them original, describes the comparative anatomy and physiology of the nose. The discussion is concerned with olfactory, respiratory, and air-conditioning mechanisms of the nose, and other functions; attention is also paid to the comparative anatomy and physiology of the paranasal sinuses. The work ends with a section on the human aspects of the nose and its accessory air chambers. It contains a wealth of authoritative information and should be welcomed by all those who have an interest in the area it covers in so scholarly a fashion.

Perspectives in Virology: A Symposium. Edited by Morris Pollard. [Third in series of scientific symposia and proceedings sponsored by Hartz Mountain Products Corporation, New York.] Cloth. $7. Pp. 312, with illustrations. Published for Institute of Microbiology, Rutgers University, by John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1959.

This book is a memorial to F. R. Beandette, a distinguished agricultural scientist. Twenty distinguished investigators present papers on different aspects of virology. These are in the nature of reviews but often include new work of the authors. Papers on basic aspects of viruses include the chemical nature of the tobacco mosaic virus, viral multiplication and transformation, nutritional requirements of viruses and cells, and cell-plating techniques. The present status of the measles virus and of 70 new human viruses, the epidemiology of influenza, and the natural history of hog cholera are brilliantly presented. Four papers on viral neoplasia outline this exciting new area. The presentations on influenza, on measles, and on the new viruses should be of special interest to the clinician. The others, while excellently done, are too technical to appeal to any but the virologists. The foreword contains a tribute to Beandette, and the epilogue a delightful piece entitled Tulipomania and the Benevolent Virus. The discussions of the papers are lively and stimulating, and there is a comprehensive bibliography for each. This is an excellent book for the graduate student and specialist in virology.

QUESTIONS AND ANSWERS

TREATMENT AND PROPHYLAXIS OF TETANUS

To the Editor:—*What dose of tetanus antitoxin should be used in treatment of a patient who has active tetanus, has not received any immunization or prophylaxis, and who had no history of injury prior to development of clinical symptoms of tetanus? Also, within what period after a tetanus booster has been given is it safe to omit another booster if a minor injury occurs such as a nail puncture or small laceration?*

John H. Cordes Jr., M.D., St. Petersburg, Fla.

Answer.—A minimum of 160,000 units and a maximum of 320,000 units of tetanus antitoxin may be used in therapy of acute tetanus. After débridement with the patient under sedation, 60,000 units is given around and proximal to the wound, if identified. The balance is given into the gluteal muscles. The dosage depends on age, sex, weight, and shortness of incubation period; the shorter the period the higher the dose. Only one sensitivity test before giving the tetanus antitoxin has proved safe: Dilute 0.1 cc. of tetanus antitoxin in 10 cc. of isotonic sodium chloride solution. Take the patient's blood pressure. Slowly inject the solution into a vein. The systolic blood pressure should not drop lower than 20 mm. Hg in a child or 30 in an adult or desensitization must be used before giving the antitoxin. The last 40,000 units of the dose selected may be given intravenously in isotonic sodium chloride, not dextrose, solution. A toxoid booster is always indicated after the type of accident mentioned. There is no contraindication.

EMERGENCY USE OF TETANUS IMMUNIZATION

To the Editor:—*In our two local hospitals we are about to adopt the following precautions against tetanus:*

1. No previous tetanus toxoid: 1,500 units of tetanus antitoxin after skin test, with larger dosage in massive wounds. It is also recommended that the patient be given 0.5 cc. of tetanus toxoid in another extremity with a second similar dose four weeks later. (This offers no protection for the current injury, but the two injections then give basic tetanus protection.)

2. Last booster dose of tetanus toxoid more than five years prior to injury: Same as above with omission of second toxoid injection, since the first injection will act as a booster to restore a protective serum antitoxin level.

3. Last booster dose of tetanus toxoid less than five years prior to injury: 0.5 cc. of tetanus toxoid.

4. Last booster dose of tetanus toxoid less than one year prior to injury: No booster required. Give booster if there is any question as to accuracy of dates.

Are there any further suggestions?

William S. Dempsey, M.D., St. Albans, Vt.

Answer.—The suggested hospital precautions against tetanus for lacerations, abrasions, burns, and puncture wounds are in accord with standard procedure. To be more conservative, the first paragraph should be changed to read 3,000 units of tetanus antitoxin instead of 1,500. The second paragraph could be modified in that for minor wounds and abrasions a prior injection of toxoid would be considered effective for 10 years. For severe or heavily contaminated injuries, however, particularly compound skull fractures, 5,000 units of tetanus antitoxin plus an additional 0.5 cc. of tetanus toxoid should be used. Paragraph 4 could be omitted altogether. Irrespective of the interval after the last tetanus toxoid booster, an additional booster should be given at the time of injury. Paragraph 3 would cover all situations not covered in 1 or 2 where toxoid had been given less than 10 years prior to injury.

MASS TETANUS IMMUNIZATION

To the Editor:—*The Morris County (N. J.) Medical Society has decided to promote mass inoculation of as many of its citizens as possible with tetanus toxoid, as was done for servicemen. Has an endeavor of this kind been carried out before? Is there any information on promotional propaganda techniques and how best to accomplish the purpose?*

Sam C. Atkinson, M.D., Summit, N. J.

Answer.—In various forms, programs for large-scale immunization of civilian adult groups against tetanus have been carried out by both formal and informal methods. The formal approaches utilize newspapers, including local weekly neighborhood publications; radio, with announcements sponsored by the local medical society; television, sponsored by the local medical society and through popular

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

news commentators; placards in buses and other public conveyances and in places where adults tend to gather in moderate to large numbers; house-to-house canvass by Boy Scouts and Girl Scouts, who distribute printed material; clinics arranged for convenience of working people, with prearranged fee schedules at a nominal level; and Parent-Teacher Association addresses.

The informal method involves the use of printed and verbal propaganda in physician's offices and hospitals. Pediatricians are strategically placed to encourage immunization of adults. The local pediatric society should be consulted in this program. Likewise, organized industry can be enlisted.

Printed material of various types is available from state health agencies, various health agencies, from various biological houses, and the several agencies associated with the National Institutes of Health, Bethesda, Md.

TOXIC NEURITIS PRODUCED BY TETANUS TOXOID

To the Editor:—*Have there been cases of toxic neuritis after inoculation for tetanus? If so, what is the proper treatment?* M.D., *Illinois.*

Answer.—This consultant has seen two cases of toxic neuritis after inoculation for tetanus. In both, the involvement was of the shoulder girdle muscles and consisted chiefly of severe motor weakness of the shoulder abductors. No specific treatment is available. Both patients were treated with vitamin B_{12} in doses of 1,000 mcg. daily. In one case the condition cleared promptly, while in the second there was 50% residual damage in spite of intensive physical therapy.

Answer.—The question does not specify the prophylactic agent employed, i. e., antitoxin or toxoid. The literature relates more to antitoxin, thus this response will be governed accordingly. The presence of extraneous materials in tetanus toxoid has allergenic potential and would be a possible factor in eliciting so-called toxic neuritis on an allergic basis.

Neuritis secondary to the administration of tetanus antitoxin includes optic neuritis (with blurring of the optic disks and gradual return to normal), involvement of the auditory nerve (marked deafness during the course of serum sickness and subsequent recovery of almost normal hearing), paralysis of the recurrent laryngeal nerve (with recovery in two to five months after onset), and peripheral neuritis of the spinal nerves, mainly those supplying the upper extremities (upper or whole brachial plexus) but not omitting those nerves derived from the lumbar plexus. The involvement may be unilateral or bilateral, and pure radial involvement may occur.

Tetanus toxoid may contain allergens. The not infrequent occurrence of serum sickness of the delayed type after tetanus toxoid administration would validate anticipation of allergic neuritis in some instances. Treatment would consist of antihistamines, steroids, corticotropin, physiotherapy, and precaution with subsequent use of the agent. Reference may be made to an article by Spaeth (*Nebraska M. J.* 41:224 [June] 1956).

TOXOID ALLERGIC REACTION

To the Editor:—*Please give information regarding allergic reaction in a patient taking tetanus toxoid immunization. The patient is a 54-year-old woman. Several years ago she apparently had a tetanus antitoxin skin test and injection to which she had an allergic reaction. She said she was told then that she would also be allergic to tetanus toxoid; however, it was recommended that she take the toxoid series and she was given 0.5 cc. of alum-precipitated tetanus toxoid. Several hours later, the patient telephoned and said she was beginning to break out with hives. She was given chlorpheniramine maleate, 12 mg. twice a day, which controlled the hives quite well. This reaction lasted with mild to moderate severity for about one week. The patient has no history of allergy other than this episode and has been in general good health. What would be the recommended procedure in immunizing this patient for tetanus?*

John A. Lauer, M.D., Clearwater, Fla.

Answer.—The circumstances would suggest that the earlier allergic reaction to tetanus toxoid was secondary to previous sensitization to some component of the preparation. In searching for this component, it would be advisable to communicate with the manufacturer to determine the materials and procedures employed in the sequences of preparation. With this information, appropriate tests for allergic hypersensitivity could provide tentative information concerning cause of the reaction. If one or multiple components should be incriminated, correspondence with other biological houses could be instituted to locate a vaccine (toxoid) not containing the noxious component(s). If such material is not available, repeated minute doses of diluted vaccine (1:1,000 to 1:100) could be administered until the tetanus antitoxin titer reaches a protective level of 0.1 unit per cubic centimeter or higher. After an initial dose of 0.5 cc. of toxoid, it is likely that several minute doses of toxoid would produce an adequate protective titer. Although the present circumstance augurs well immunologically for a minute additional dose of tetanus toxoid (because of a relatively large initial dose of 0.5 cc.), less favorable circumstances would permit the induction of active immunity on the basis of repeated minute doses of toxoid, guided by titrations of the subject's blood serum after five or more doses of 0.1 cc. of 1:1,000 to 1:100 dilutions of tetanus toxoid. Such a procedure utilizes the principle of "immunological momentum" (Spaeth, *Nebraska M. J.* 42:112, 1957). To protect against acute anaphylactic shock, dosage with a 1:1,000 solution of epinephrine hydrochloride should be provided with each injection and antihistaminic drugs should be prescribed. Arrangements should be made with the biological house for titration studies.

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Northwestern University
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"There would appear to be no sound reason for encouraging the establishment of pension plans for the employes of business organizations without providing the same encouragement for the establishment of plans for those who employ themselves," he testified. With the number of aged citizens increasing, "it would seem prudent and logical to act now to encourage additional people to provide for themselves the security they will need after they have reached retirement age and have lost all or part of their earning power."

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This estimate assumes that the self-employed will invest 1 billion dollars in retirement plans the first year, he said, adding that "there is little reason to assume that a million self-employed will immediately deposit $1,000 each under this plan. Indeed, surveys indicate that only about 50% of the self-employed intend to utilize the plan at all."

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

"Lack of information about hazardous ingredients in cases of poisonings have enhanced their gravity by complicating or delaying treatment," said Dr. Blasingame. "The law should require informative labeling, which would include a list of hazardous ingredients, their potentialities for harm, directions for safe use, and first-aid instructions."

Dr. Blasingame called for clear, outstanding warning symbols to facilitate recognition, declaring that in practice few persons are sufficiently impressed by such words as "danger," "warning," or "caution." Consideration should be given, he said, to the use of such familiar warning symbols as a flame for inflammable substances and a skull and crossbones for poisonous substances. Different pictorial symbols should be used according to the danger of the products, he said.

The measure before the Committee should be broadened to apply to all hazardous substances "distributed as packaged chemicals for nonmanufacturing purposes," rather than simply to those "intended or suitable for household use," said Dr. Blasingame.

He noted that the A. M. A.'s Committee on Toxicology had spent two years studying the problem and made recommendations concerning the need for more sweeping labeling requirements.

INCIDENCE OF POLIOMYELITIS RISES

Although the rate of climb has diminished, the number of paralytic poliomyelitis cases continued to rise through the week ending Aug. 1, with 183 cases reported to the U. S. Public Health Service. This was a weekly high for the year.

The 183 cases compared with 175 cases the week before and 166 the previous week when there was a 50% jump in cases.

Through the month of July 1,134 paralytic polio cases were reported, in contrast to 579 during the same period last year and 2,525 in 1955 before Salk vaccine was in widespread use.

The latest cases represented small clusters in most parts of the country, said PHS, with the exception of New Haven, Conn., which was classified as the only epidemic area.

From the first of the year through Aug. 1, drug manufacturers produced 50,764,371 doses of vaccine, compared with 47,141,871 doses during the same period last year.

NURSING HOME AID AGAIN VOTED

The program to encourage construction of proprietary nursing homes survived maneuvers in a political tug of war between Congress and President Eisenhower on housing legislation.

After the Senate failed to override the chief executive's veto of a previous housing bill, the Senate Banking Committee approved a $1,050,000,000 program, scaled down from the 1.4-billion-dollar bill that was vetoed.

The bill was identical to one cleared by a Senate banking subcommittee, except for a change in the method of financing a college classroom program.

The new measure provided Federal Housing Administration loan guarantees for construction of proprietary nursing homes.

The noncontroversial loan guarantee program, backed by the American Medical Association, was part of the vetoed bill as well as the compromise measure. The full Banking Committee had first decided by an 8 to 7 vote to attempt to override the veto and, when this was unsuccessful, voted the compromise.

Other sections of the housing measure of interest to physicians would provide $62,500,000 for interns' and nurses' housing under the college housing program, and establish a 50-million-dollar revolving fund for direct loans to help private nonprofit corporations build rental housing for the elderly. The Banking Committee trimmed the $62,500,000 for interns' housing to 25 million dollars, but did not change the provision on housing for the elderly which President Eisenhower had criticized in his veto message.

SCHEDULE FOR HEARINGS ON AGED TENTATIVELY SET

The special Senate labor subcommittee investigating problems of the aged planned more than a month of hearing in cities across the country after Congress adjourns.

Sen. Pat McNamara (D., Mich.), Chairman of the group, said he would call witnesses to testify on all aspects of aging, including medical care, finances, and employment policies.

Cities under consideration for subcommittee visits included Detroit, Grand Rapids, and Lansing, Mich.; San Francisco; Miami, Fla.; Boston; and cities in Pennsylvania and West Virginia. The sessions will begin the second week in October and continue into the month of December.

MISCELLANY

U. S. Surgeon General Leroy E. Burney appointed an ad hoc committee of 10 state health officials and 2 representatives of the Public Health Service "to develop a basis for improved planning of mental health facilities throughout the nation." Dr. Burney said the committee was formed in response to a recommendation of state health authorities.

Major Gen. Leonard D. Heaton, surgeon general of the Army, was nominated by President Eisenhower for promotion to Lieutenant General. The 56-year-old officer's nomination is subject to confirmation by the Senate.

Public Health Service awarded $11,200,000 in grants to help build and equip additional health research facilities in 47 institutions. The grants are designed to improve and expand the nation's facilities for medical and dental schools, schools of public health, and other research institutions. Largest grants were $1,297,955 to the University of Oregon medical school, and $1,292,975 for the University of California.

A new, agency-wide committee was established by the Veterans Administration to make a sweeping study of medical, social, and economic problems of aging veterans. VA Deputy Administrator Bradford Morse will head the committee. The VA pointed out that, in 12 years, 16 million of 22 million veterans of World War II will be over 45 years of age.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

August

American Association of Electromyography and Electrodiagnosis, Mayo Clinic, Rochester, Minn., Aug. 29-30. Dr. Edward Lambert, Mayo Clinic, Rochester, Minn., Program Chairman.

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Mississippi Valley Medical Society, Hotel Chase, St. Louis, Sept. Oct. 1. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Execu Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgec Chicago, Sept. 13-17. For information write the Secretariat, 1516 L Shore Dr., Chicago 10.

Ohio Society of Anesthesiologists, Dayton Biltmore Hotel, Dayton, S 18-19. Dr. Nicholas G. DePiero, 9710 Garfield Blvd., Garfield I 25, Ohio, Secretary.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23- Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Execut Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28- Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Te Chairman.

United States Section, International College of Surgeons, Pal House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Sh Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt L City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake Cit Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, S 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Execut Secretary.

Western Neurosurgical Society, La Valencia Hotel, La Jolla, Cal Sept. 27-30. Dr. Ernest W. Mack, 505 S. Arlington Ave., Reno, N Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cle land, Oct. 15-17. For information write: Dr. Bertram B. Moss, Su 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, T Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 S ond St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, O 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, I Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hot Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Ro 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hot Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn S Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Philad phia, Oct. 23-25. Dr. Philip Reichert, Empire State Bldg., New York Executive Director.

American College of Chest Physicians, 25th Anniversary Homeco ing Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfel 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, A lantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 126 Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philade phia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New Yo 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, O 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conr Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lan Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hot Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic Cit N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New Yo 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic Cit N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohi Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, B Harbour, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-17 Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Hote Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray Broad bent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Hotel Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road Miami 33, Fla., Executive Secretary.

Association of Clinical Scientists, Sheraton-Park Hotel, Washington D. C., Oct. 10. Dr. Robert P. MacFate, 323 Northwood Rd., Riverside Ill., Secretary-Treasurer.

Association of Life Insurance Medical Directors of America, Hote Statler Hilton, New York City, Oct. 21-23. Dr. Royal S. Schaaf, Prudential Insurance Co., P. O. Box 594, Newark 1, N. J., Secretary.

Association of Medical Illustrators, Seattle, Oct. 5-7. Miss Rose M. Reynolds, University of Nebraska College of Medicine, 42nd Dewey Ave. Omaha 5, Corresponding Secretary.

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INTRAFAMILIAL AND INTERFAMILIAL SPREAD OF LIVING VACCINE STRAINS OF POLIOVIRUSES

Henry M. Gelfand, M.D., Louis Potash, Ph.D., Dorothy R. LeBlanc, R.N.
and
John P. Fox, M.D., Ph.D., New Orleans

Fifty-six household units participated in a study of the spread of poliovirus within families and between families. Within this group all persons above the age of 6 months and not naturally immune had previously received the Salk vaccine. Each of the families used included at least three naturally susceptible members. Sabin vaccine was administered by squirting 1 ml. of the single-strain virus suspension into the back of the recipient's mouth. All but one adult was successfully infected after receiving the recommended dose. Virologic and serologic methods demonstrated transmission to many contacts, fecal excretion of the virus being the most sensitive indicator of that fact. The virus commonly appeared in the pharyngeal secretion within the first two days. The most important factor favoring intrafamilial transmission was low socioeconomic status. No evidence was found to suggest that any illness, however minor, followed the administration or spread of any of the three vaccine virus strains used.

With the isolation, selection, purification, and large-scale production by Koprowski,[1] Sabin,[2] and Roca-Garcia and others[3] of attenuated variants of polioviruses of all three types, we are offered the opportunity to substitute live-virus vaccination against poliomyelitis for the formalin-inactivated vaccine in current use.

Among the generally accepted advantages of vaccination with the infectious strains we may list (1) the ease of administration: oral versus parenteral administration; (2) the duration of protection: theoretically life-long; (3) the percentage of effectiveness: perhaps close to 100% versus the 70 to 80% now attained by Salk vaccine; (4) the rapidity of effective immunization: making possible its use in established epidemics; and (5) the "herd" immunity produced: by inducing local intestinal resistance. The generally recognized disadvantages include (1) the necessity for an interval of some weeks between the administration of the different types and (2) the danger of accidental contamination of the vaccine by other living microbial material. The latter danger can be obviated by proper care during production and safety testing afterward, and the former may be overcome by future technical development.

A controversial characteristic of live-virus poliomyelitis vaccination is the ability of these strains to be transmitted from the vaccinated person to his

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contacts. The very earliest work with living attenuated polioviruses showed that, some days after oral administration, they are excreted in the feces. Subsequently, Koprowski and others,[4] Dick and others,[5] Horstmann,[6] Martins da Silva and others,[7] Smorodintsev,[8] Sabin,[9] and Gard,[10] using various strains of all three types, have unequivocally demonstrated spread to susceptible persons under various conditions of contact. In itself, the occurrence of this phenomenon probably would be of little concern, were it not for the possibility that the fecally excreted viruses being spread may have undergone back-mutation to a level of neurovirulence greater than was acceptable in the original oral vaccine. One might well take the even more extreme position that, were it not for this possibility of back-mutation, spread of vaccine viruses by contagion is a decided advantage of live-virus vaccination, in that the administration of vaccine to only a portion of the population might result in the effective vaccination of the entire population. This would be vaccine-induced "herd protection" of a level not yet achieved with any immunizing agent.

The demonstrated tendency of attenuated strains of poliovirus to change in the direction of increased virulence on multiplication in the intestinal tract may have little practical significance in human beings, but a final conclusion is as yet unwarranted. Intraneural tests of the excreted viruses have yielded inconsistent results in the hands of different investigators and, moreover, no one has ventured to suggest what the maximum tolerable reversion might be. Regardless of the eventual result of this disagreement, knowledge of the infectivity and transmissibility of the vaccine strains is essential to their rational use in field trials and, eventually, in routine practice. The present communication will report, in preliminary fashion, the results of studies on the capacity of a set of vaccine strains to spread within families living under normal conditions in southern Louisiana.

Material and Methods

Population Studied.—Families for the present investigation were recruited in 1958 from a group in New Orleans which had been under our observation from 1953 through 1957 in a study of natural infection with polioviruses.[11] Their infection history was therefore unusually well known. During 1956 and 1957 all persons above the age of 6 months and not naturally immune to all three poliovirus types had been given three suitably spaced inoculations with Salk vaccine. Infants who were under 6 months of age at the beginning of this study were not vaccinated after it began.

To be eligible for the present purpose, a family had to include, for any given type, at least three "naturally susceptible" members, defined as persons without prior natural homologous infection as observed by us and coupled with the complete absence of naturally acquired serum-neutralizing antibody as measured by the direct cytopathic test. On this basis, a family might be "eligible" for more than one type, and many were used two or three times. Each feeding and family observation was therefore designated as a separate "unit" and so reported below. In addition, in several instances the same virus type was fed more than once in a single household when the first failed to cause infection and/or spread. Again, each feeding was considered a separate unit of study. On a few occasions, the vaccine was purposefully fed to naturally immune persons in households which also contained two homologously susceptible persons as indicators of spread. These units are separately considered. Family units were assigned to one of three socioeconomic categories: Caucasian–upper economic, Caucasian–lower economic, and Negro. The Caucasian group was divided on the basis of an aggregate family income of $3,500 per year (in 1953), and all Negro families fell below this level. Although arbitrary, this economic division was rather well correlated with social and sanitary facilities and practices such as household crowding, adequacy of toilet and hand-washing equipment, and "personal hygiene." Since there has been no prior evidence that race as such plays any part in the transmission of polioviruses, units usually are combined below only as upper economic or lower economic.

Virus Strains and Vaccine Administration.—The viruses used were kindly provided by Dr. Albert Sabin and were from single large pools of each type that had fulfilled his rigid criteria for purity and attenuation.[2] These strains were designated L Sc, 2 ab (type 1), P 712, Ch 2 ab (type 2), and Leon 12 a_1b (type 3). The stock material, undiluted or diluted as necessary with Hank's balanced salt solution, was distributed in 1.2-ml. aliquots into individual screw-topped vials, which were then kept at −20 C until used. The doses fed were calculated to contain approximately 100,000 (5 log doses) or 10,000,000 (7 log doses) infectious particles. Repeated titration of sample vials in cultures of rhesus kidney cells showed that actually an average of 5.3 and 7.3 log doses (type 1) and 5.1 and 7.1 log doses (types 2 and 3) had been used although, by error, a few persons received 3.6 log doses (4,000 infectious units) early in the study. These figures may need some upward revision for, in a recent communication, Sabin [9] reports that higher titers of his vaccine pools may be obtained by titration in cynomologous kidney-cell tissue cultures and an improved technique. Consequently, the doses we used may have been greater than reported here, i. e., approximately 4.3, 6.0, and 8.0 log doses (type 1), 5.3 and 7.3 log doses (type 2), and 3.9, 5.4, and 7.4 log doses (type 3).

Administration of the Sabin vaccine was done in the recipients' homes by one of us (D. R. L.) by squirting 1 ml. of the single-strain virus suspension into the back of their mouths, after which they drank a glass of water. The vials of vaccine were carried into the field on ice, and were never used for more than six hours from the time of leaving the laboratory. Several titrations of vials returned to the laboratory after that time showed that no significant titer decline had occurred. Individual medicine droppers were used in administration, and extreme care was taken to prevent contamination of the skin of the recipient or of objects in the home.

Method of Study and Collection of Specimens.—For each family unit of study, one susceptible person was chosen for administration of the homologous type of vaccine virus and was designated the "index" person. The two or more other susceptible persons and the naturally immune household members were all observed as "family contacts." In a few instances, observations were made on the possible spread of these viruses to other persons not living in the same domicile who are referred to as "extra-household" contacts.

TABLE 1.—*Schedules of Specimen Collection*

Donors	Type of Specimen	Days After Vaccine Feeding on Which Indicated Specimens Were Collected		
		Complete Schedule	Modified Schedule	Abbreviated Schedule
Index person	Blood	0, 3, 7, 11, 14, 18, 21, 60	0, 8, 20, 60	0, 60
	Pharyngeal	0-11	0, 2, 4, 8	None
	Fecal	0-14, 18, 21, 25, 28; 1 x per wk. to termination	0, 2, 4, 8; 1 x per wk. to termination	0; 1-2 x per wk. for variable period
Family contacts	Blood	0, 60	0, 20, 60	Same as index
	Pharyngeal	3-17	0	
	Fecal	0, 3-17, 21, 25, 28, 31; 1 x per wk. to termination	Same as index	
Extra-household contacts	Blood	0, 60	None	None
	Fecal	7, 14, 21		
No. of household units completed by indicated schedule		26	17	8 (plus 5 immune feedings)

The various schedules of specimen collection are outlined in table 1. Day "0" is the day of feeding in all instances. These schedules were set up as guides only and were often modified to suit the individual situations found in many households.

Blood specimens were almost always collected by venipuncture, with use of vacuum bleeding tubes; less than 1% were by heel puncture in small infants. Pharyngeal specimens were obtained from adults and older children by gargling. Screw-topped ointment jars were prepared with 7 ml. of tissue-culture maintenance fluid; this provided the gargle fluid, and it was expectorated back into the same container. With small children, the tonsillar area and posterior pharynx were thoroughly swabbed with a dry cotton-tipped applicator, and the latter was then dropped into a tube containing 5 ml. of maintenance fluid. Fecal specimens consisted of a pellet of whole feces placed into an ointment jar. Specimens were held at refrigerator temperature, usually no longer than overnight, before processing in the laboratory.

During the investigation of a number of family units, an attempt was made to detect the presence of poliovirus on the skin of the hands and buttocks of some children, and on the floor, on toys, and on other fomites. For this purpose, cotton pledgets wetted with Hank's solution were swabbed over the appropriate surface and returned to the laboratory, where they were squeezed almost dry. The resulting fluid was treated as indicated below for fecal extracts and pharyngeal gargles.

Laboratory Procedures.—Rhesus monkey kidney-cell tissue cultures, prepared in this laboratory, were employed throughout, with use of techniques now standard.[11]

For virus isolation, stool specimens were processed into 10 to 20% fecal extracts containing penicillin, streptomycin, and nystatin (Mycostatin), while pharyngeal specimens were used as collected, after centrifugation and the addition of antibiotics. Each of four tissue-culture tubes was inoculated with 0.25 ml. of each specimen. The latter were incubated at 37 C and examined at intervals for 10 to 13 days, with a change of lactalbumin maintenance medium fluid on the fourth to seventh day. Specimens were recorded as negative if there was no evidence of a cytopathic effect after this time; if doubtful, the supernatants were pooled, and a subculture was made by inoculating 0.1 ml. of the pooled material into each of two new tubes which were then incubated for four to seven days. When a cytopathogenic agent was recovered, identification was first attempted by neutralization with hyperimmune rabbit antiserum prepared against the virus of the type fed. If complete neutralization did not occur, further investigation was made with the use of polyvalent serums against the other types of polioviruses, Coxsackie viruses A9 and B1-5, and ECHO types 1 to 14, followed by the appropriate monotypic tests.

Serums were tested for the presence of neutralizing antibody in the direct cytopathic test for the high-avidity antibody of Sabin.[9] Aliquots of each serum dilution were incubated for one hour at room temperature, with an equal quantity of virus suspension calculated to contain approximately 100 tissue culture infective doses ($TCID_{50}$) per 0.1 ml. For index persons, four tubes were used per twofold dilution and for contact persons, two tubes per twofold dilution. End-points are expressed as of the final serum dilution.

Results

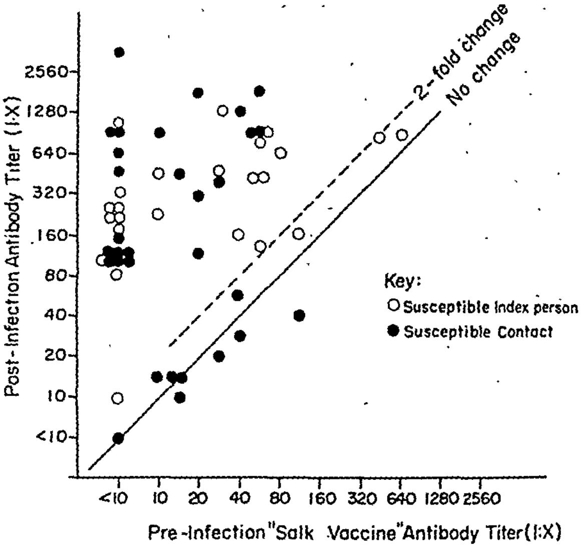
The available data relating to 56 family units are the subject of this preliminary report. In 51 units, a naturally susceptible person was fed, the distribution of these by socioeconomic and family status being as follows: Negro, 13 children only; Caucasion-lower economic, 13 children only; and Caucasian-upper economic, 18 children and 7 parents. In five additional units, a homologously naturally immune index person was fed.

Infections in Susceptible "Index" Persons.—Of the 51 feedings represented by these household units, all but five resulted in the infection of the index person, as indicated by the subsequent recovery of homologous virus from the pharyngeal and/or fecal excretions. As may be seen in detail in table 2, four of these failures were in persons who had received the small 3.6 log dose of type 1 vaccine. One of the four failures was an adult, who was then refed with 5.3 log doses of the same virus type. Again he failed to become infected, representing the fifth and last feeding failure. He was refed once more, with 7.3 log doses of the same type, and thereupon excreted virus fecally for five days.

Table 2.—*Summary of Efforts to Recover Virus from Pharynges and Feces of Index Persons Fed "Sabin Vaccine," by Virus Type, Dose, and Family Status*

			Homologous Virus Detected in Appropriately Collected Specimens			
			Pharyngeal		Fecal	
Vaccine Virus, Type	Dose Fed, Log	Family Status	No. of Persons Examined	No. of Persons Positive	No. of Persons Examined	No. of Persons Positive
1.....	3.6	Child (2-8 yr.)	3	0	3	0
		Adult	1	0	1	0
	5.3	Child (2-8 yr.)	4	1	6	6
		Adult	2	0	2	1
	7.3	Child (2-5 yr.)	6	5	6	6
		Adult	1	1	2	2
2.....	5.1	Child (2-6 yr.)	5	0	6	6
		Adult	0	—	0	—
	7.1	Child (2-6 yr.)	7	4	8	8
		Adult	1	1	1	1
3.....	3.6	Child (1-2 yr.)	2	0	2	2
		Adult	0	—	0	—
	5.1	Child (3-7 yr.)	5	0	6	6
		Adult	0	—	0	—
	7.1	Child (2-6 yr.)	6	5	7	7
		Adult	1	0	1	1

Among the 46 persons who did become infected, fecal excretion was the most sensitive indicator of that fact. Pharyngeal excretion was usually detected after the administration of 7.1 to 7.3 log doses (16 of 22 persons examined), but was found after 5.1 to 5.3 log doses in only 1 of 16 persons examined. The serologic detection of infection, as indicated by a titer rise fourfold or greater, was even less reliable. Study of appropriate specimens of all persons is not yet complete, but as indicated in the figure, significant rises above the titers persisting from Salk vaccination completed one to two years previously often failed to occur where the titer before infection was greater than 1:40. It must also be added that in no instance did a significant serologic titer rise occur in any person from whose fecal specimens we failed to isolate virus. It may also be seen in table 2 that the age of the index person did not appear to affect the likelihood of infection after feeding with any given virus type or dose.



Homologous antibody titers before and after proved infection with "Sabin vaccine" in naturally susceptible persons.

The duration of excretion was very variable; demonstrable excretion from the pharynx lasted from a minimum of 2 to a maximum of 17 days and, in the feces, from a minimum of 2 to a maximum of at least 137 days. There appeared to be no relationship between this duration and either the size of the infecting dose or the age of the recipient. Table 3 shows the distributions and means of the durations

Table 3.—*Duration of Pharyngeal and Fecal Excretion of Polioviruses After Oral Administration of "Sabin Vaccine"*

	No. of Persons with Indicated Duration After Ingestion of Indicated Virus Type					
	Type 1		Type 2		Type 3	
Observed Duration of Excretion, Days	Pharyngeal	Fecal	Pharyngeal	Fecal	Pharyngeal	Fecal
1....................	0	0	0	0	0	0
2....................	0	1	1	0	0	0
3....................	0	0	1	0	0	0
4....................	1	0	0	0	0	0
5....................	0	1	0	0	0	1
6-10................	4	4	3	5	3	0
11-15................	1	1	0	1	1	2
16-20................	1	3	0	2	1	2
21-30................	0	2	0	2	0	3
31-40................	0	2	0	3	0	3
41+..................	0	1	0	2	0	5
Mean duration......	8.8	24.7	4.8	24.9	10.1	31.5
Mean interval*......	1.9	4.8	1.8	5.3	1.8	4.2

* Average time elapsed between last negative specimen before excretion began and last positive and first negative specimen after excretion ended.

of excretion after ingestion of the three virus types of vaccine. (The means of the intervals between the last negative specimen before excretion began and the last positive and the first negative after it ended are given to show the equivalence of the observations.) There is a suggestion that the excretion of type 3 virus may last longer than that of the other types, although the record in this series, 137 days with no end-point being reached, was with type 1.

The incubation period of infection, as measured by the interval between the ingestion of vaccine and the onset of continuous excretion of homologous virus, was very short in the majority of index persons on whom daily observations were made. Of 11 persons in whom pharyngeal excretion was systematically sought, three were excreting virus within one day, six by the end of the second day, and in only one each was excretion first detected on the third and fifth day respectively. Of 27 persons examined daily for the presence of virus in the feces, 17 were found to be excreting within one day, nine others by the end of the second day, and in only one was onset delayed until the fifth day. There was no suggestion of a relation to virus type or dose.

Table 4.—*Homologous Infections Occurring Among Family Contacts of Index Persons Infected After Oral Administration of "Sabin Vaccine"*

Natural Immunity Status of Family Contacts	Family Status of Index Person	Virus Type	Contacts in Upper Economic Family Group Occurrence of Pharyngeal Virus Excretion in Index Person				Contacts in Lower Economic Family Group Occurrence of Pharyngeal Virus Excretion in Index Person			
			Yes		No		Yes		No	
			No. of Units	Ratio* of Contact Infections	No. of Units	Ratio* of Contact Infections	No. of Units	Ratio* of Contact Infections	No. of Units	Ratio* of Contact Infections
Susceptible	Child	1	4	2/9	3	1/6	2	2/6	3	5/9
		2	1	0/2	2	0/5	4	9/11	9	3/22
		3	1	0/2	5	1/20	5	13/15	4	7/11
	Parent	1	2	0/5	1	0/3	—	—	—	—
		2	1	0/3	—	—	—	—	—	—
		3	—	—	1	0/3	—	—	—	—
Immune	Child	1	4	2/8	3	1/7	2	1/6	3	1/6
		2	1	0/2	2	0/2	4	3/14	8	3/17
		3	1	0/3	5	0/6	5	9/21	4	2/11
	Parent	1	2	0/2	1	0/1	—	—	—	—
		2	1	0/1	—	—	—	—	—	—
		3	—	—	1	0/1	—	—	—	—

* Ratio of persons infected (numerator) to family contacts present in home (denominator).

Complete series of blood specimens were collected from 16 of the susceptible index persons on days 0, 3, 7, 10, 14, 17, 20, and 60. Rise in neutralizing antibody titer, observed in 15 of these susceptible index persons, occurred between the 7th and 10th days in 12 instances, and between days 3 and 7 or 10 and 14 in two and one cases respectively. The antibody titer had clearly begun to decline between days 20 and 60 in 10 of these 15 persons.

Two susceptible index feedings are worth noting in detail. Reference has already been made to an adult who failed to become infected after ingesting 3.6 and 5.3 log doses of type 1 Sabin vaccine, but then excreted virus in the feces for five days after the administration of 7.3 log doses. It was felt that this man may have been naturally immune without demonstrable neutralizing antibody. One child was also fed more than once. After ingestion of a 3.6-log dose of type 3 Sabin vaccine, she had five days of fecal excretion but no serologic response. She was refed with a 5.1-log dose of the same type, whereupon she excreted for 29 days and experienced a marked rise in antibody titer from 1:56 to 1:800. The first infection in this child may represent the implantation of virus in so limited an area of the intestine that full evolution of the infection did not occur, and the antigenic stimulus thus was too weak. Thereafter, she remained fully susceptible, and acted as a nonimmune person on reexposure.

Infection Attempts in Naturally Immune Index Persons.—Only five naturally immune persons have so far been completely studied after ingestion of Sabin vaccine. Three of these were fed type 1 virus, and each of the others was fed type 2 or 3. All were children, and all were fed the larger dose. Three of the five failed to become reinfected. One child excreted type 1 virus in the feces for nine days, but failed to excrete from the pharynx; the child fed type 2 virus also excreted fecally for nine days, but no pharyngeal specimens were collected. Serums have not yet been tested.

Spread of Infection from the Index Person to Family Contacts.—Because of the large number of variables, any or all of which may significantly influence the spread of vaccine viruses within household units, the combination of units with identifiable differences is not fully justified. Table 4, therefore, reports the ratio of infections among naturally susceptible and naturally immune family contacts within the few units included in each category as defined by virus type, presence or absence of pharyngeal virus excretion, economic status, and family status of the index person. Since the dose of attenuated virus fed was not demonstrated to have an effect in the infected index person other than determining the likelihood of the occurrence of pharyngeal excretion, distribution of the results by dose was not tabulated. The determination of contact infection was based, in all cases, on the occurrence of fecal excretion.

Examination of this table shows a number of interesting contrasts. Among the susceptible family contacts of infected index children, many infections occurred, but there was a marked difference based on economic status, the families from the lower economic group experiencing many more. Among the three virus types of the Sabin vaccine, type 3 feedings appeared to have resulted in more spread. The presence of pharyngeal excretion may have been associated with more extensive spread than occurred in its absence, at least with types 2 and 3 virus, although a number of these contact infections apparently took place long after pharyngeal excretion had ceased. Despite the fact that the observations were few in number and restricted to families from the upper economic group, it is striking that no single instance of spread followed the infection of an index adult, even though several experienced prolonged pharyngeal excretion. Finally, the rather large number of reinfections among naturally immune persons is notable.

Table 5.—*Summary of Homologous Infections Occurring Among Family Contacts of Infected Index Children, by Economic Status and Virus Type*

	Upper Economic Family Group		Lower Economic Family Group	
Virus Type	Ratio* of Contact Infections	% of Contact Infections	Ratio* of Contact Infections	% of Contact Infections
	Susceptible Contacts			
1	3/15	20	7/15	47
2	0/7	0	12/33	36
3	1/22	5	20/26	77
All	4/44	9	39/74	53
	Immune Contacts			
1	3/15	20	2/12	17
2	0/4	0	6/31	19
3	0/9	0	11/33	33
All	3/28	11	19/76	25

* As in table 4.

Since differences based on economic status and virus type appeared to have been the most significant, a summary of homologous infections among the contacts of index children is shown in table 5. With the larger numbers of subjects now available, the "benefit" of lower economic status and the generally greater infectiousness of type 3 vaccine are more evident. Type 2 appears to have been the least infectious. No family contact infections resulted from the two successful feedings in naturally immune persons with types 1 and 2 viruses respectively.

The less frequent collection of stool specimens from contacts renders difficult exact statements about the interval of time between the onset of viral excretion in the index person and that in his contacts. On several occasions, however, it was as short as one day, and on others not before one, two, or three weeks. It was particularly notable that viral excretion by naturally immune persons was often greatly delayed. The infection records of two typical families from the lower economic group are reproduced in table 6.

Spread of Infection of Extra-Household Contacts.—An adequate record of specimens from persons outside the home who were in contact with Sabin vaccine-infected families is available in connection with only four study units, since extra-household studies were initiated only where conditions for spread were likely to be optimal, i. e., with the administration of 7 log doses in lower economic families. In one of these units, neither the two siblings within the family nor the one susceptible extra-household child contact became infected with type 2 poliovirus, despite prolonged fecal excretion by the index child and frequent, intimate contact.

The second of the units studied was remarkable in that a single 2-hour period of contact, confined exclusively to the type 3–infected index child, resulted in the infection of two out of three child visitors. The third unit is in some contrast in that a similar two-hour contact period between three child visitors and the four infected children in the family studied resulted in only one infection. The two who missed infection had the same limited opportunity two weeks later and again escaped.

A special study was planned around a fourth unit which was intended to initiate a long series of passages from one household to another, among a group of cooperative, related families. The index child was fed type 3 Sabin vaccine and then removed from all play contact, except with her siblings; on infection of the four siblings, only the latter were permitted to associate with the extra-household families. The second link in the intended series was a large family containing five susceptible cousins. Unfortunately, this passage failed completely, despite frequent and intimate play contact, perhaps because of interference by coincidental natural episodes of ECHO type 1 and poliovirus type 2 involving four of the five type 3–susceptible children in the exposed household. However, three of the four other extra-household contacts in three households did contract infection with type 3.

Nature of the Infection Experienced by Contacts.—Only on a single occasion was homologous virus isolated from the pharyngeal specimen of a contact. The distributions and means of the durations of fecal homologous polioviral excretions, by contacts of persons ingesting Sabin vaccine, are indicated in table 7.

The significance of the shorter mean duration of type 1 excretion is doubtful, in view of the great variation among individuals and the small numbers involved. Of greater import is the rather large number of contact persons who excreted for very short periods of time, and who were therefore unlikely to be able to spread their infections to others. This is particularly characteristic of those naturally immune, but is also true of a substantial proportion of the naturally susceptible contacts. Since all of the persons who excreted for only one day also failed to experience a booster rise in high-avidity antibody titer, and since, in many instances, fecal specimens were not obtained daily from contacts (table 6), it is quite likely that a number of contact infections with only brief viral excretion were missed. It is interesting, nevertheless, that the mean duration of excretion of all three types among susceptible contacts (24.3 days) was very close to the same mean among susceptible index persons (28.2 days).

The likelihood of detecting a titer rise after proved infection in those persons who had preexisting antibody derived from Salk vaccine was previously discussed and illustrated in the figure. The more frequent absence of rise from low initial titer in infected contacts, as compared with infected index persons, is notable and related to the frequency of transient infections in the contacts. Among the 14 naturally immune persons in whom infection was observed and whose serums have been studied, no rise in titer could be demonstrated.

TABLE 6.—*Sample Families to Illustrate Spread of "Sabin Vaccine" After Administration to Single Naturally Susceptible Index Child*[*]

Family Status	Age, Yr.	Homologous Natural Immunity Status[†]	Homologous Antibody Titer 1:x on Day		Presence of Homologous Virus in Feces on Day														
			0	62	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
		Unit 6: Negro, Index Fed 5.3 Log Dose of Type 1 Virus																	
Father	...	I	640	320	−	−	−		−		−		+	+		−			−
Mother	...	I	80	160	−		−		−				−	−	−				−
Children	12	S	28	20	−			−		−		−	−		−			−	−
	9	S	28	20	−	−		−		−	−				−			−	
	8	S	10	14	−		−	−		−			−	+			−		−
	7	S	20	320	−	−			−		+		+		+		+		
	5	S	<2	10	−	−		−			+	−		−			−		−
⟶	3	S	10	220	−	−[‡]		+			+	+		+				+	
	1	S	<2	640	−		−	−		−		−		+			+		+
		Unit 39: Caucasian-Lower Economic, Index Fed 5.1 Log Dose of Type 3 Virus[§]																	
Father	...	I	20	14	−	−						−			+				
Mother	...	I	28	20	−	−				−		−			−				
Children	11	I	450	640	−		−			−		+		−			+	−	
	9	I	160	160	−		−	−		−		+	−		+				+
	6	S	5	110	−	−		−			+		+					+	
	5	S	<2	110	−	−	+			−	+	+	−				+		
⟶	3	S	<2	160	−	+[‡]	+			+	+			+			+		
	2	S	<2	110	−		+			−		+		+	+	+		+	

[*] "+" indicates virus isolation; "−" indicates no virus isolation from available specimens; and no symbol indicates no specimen collected. "Index" child indicated by arrow.

[†] I = immune; S = susceptible.

[‡] No virus isolated from pharyngeal specimens collected on day 1 through 10.

[§] On 13th day homologous poliovirus was isolated from kitchen floor.

Coincidental "Wild" Enteroviral Infections.—Since many of the family units of study were being investigated during the summer and autumn months, and since New Orleans is an area of high enteroviral endemicity, it is not surprising that several episodes of infection with other enteric viruses occurred coincidentally with the administration of the Sabin vaccine: poliovirus type 2, ECHO virus types 1, 6, and 9, Coxsackie virus types A9 and B5, and an unidentified agent with adenovirus-like cytopathogenicity. On several occasions, interference between these agents and attenuated strains being fed was strongly suggested. Table 8 gives three examples. In unit 10, Coxsackie B5 was infecting all three susceptible children at the time when type 1 Sabin vaccine was fed to the 5-year-old. The large dose administered may have suppressed further multiplication of the Coxsackie virus in the index child, but the smaller dose received by the others by way of "normal" contamination appears not to have been sufficient, and they escaped "vaccination." Unit 15 may illustrate reciprocal interference between a "wild" type 2 and the attenuated type 1 virus. At a later time, after both types had disappeared from the family, the index child became infected with type 2, perhaps from a neighborhood source outside the home. In unit 46, an ECHO type 1 episode was either just beginning or nearing termination in the household when the index child was fed with attenuated type 3 Sabin vaccine. The ECHO infections spontaneously disappeared or were suppressed by the spreading attenuated poliovirus, and eventually all susceptible children became infected. In addition to other episodes similar to the above, many casual infections with enteroviruses, including an ECHO 9 isolation from a pharyngeal gargle, were detected later during the course of unit investigations, when interference could not be postulated.

Virus Recovery from the Skin and from Fomites in Households.—During the course of the investigation of 26 study units, some attempt was made to detect the presence of homologous poliovirus from sites other than the pharyngeal or fecal excretions during that period after vaccine administration when the virus was circulating widely among family members. This effort was opportunistic, not carefully organized, and was made in those households with the poorest hygienic standards where the likelihood of environmental contamination was greatest. The places examined by swabbing included most commonly the skin of the hands, feet, and buttocks (excluding the perianal area) of an index child or his infected siblings, toys, floors, and doorknobs.

Table 7.—*Duration of Fecal Excretion of Homologous Polioviruses by Family Contacts of Persons Fed "Sabin Vaccine"*

Observed Duration of Excretion, Days	No. of Family Contact Persons					
	Immune			Susceptible		
	Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
1	4	3	5	4	0	3
2	1	2	0	0	1	0
3	0	0	0	1	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6-10	0	1	3	1	1	3
11-15	0	0	0	0	4	1
16-20	0	0	0	0	1	4
21-30	0	0	2	1	0	0
31-40	0	0	1	2	3	2
41+	0	0	0	1	2	6
Mean duration	1 2	2.7	9.8	16 0	27.0	27 0
Mean interval*	6 6	2 3	4 3	5 9	3 9	5.8

* As in table 3.

In five study units a poliovirus was recovered. In one instance the homologous type 2 was collected from the buttocks of the index child, and in two other instances the homologous type 3 was found on the buttocks of an infected sibling or on the kitchen floor. In a fourth unit, the homologous type 3 was recovered from the hands of the index child in four separate attempts on different days. The fifth instance is most interesting in that in a family fed Sabin vaccine type 1, which experienced a coincidental "wild" type 2 poliovirus infection, only the latter virus was found in a swab of the living room floor.

Illness Associated with Infection with Attenuated Vaccine Viruses.—Despite intensive and leading questioning, no evidence could be found to suggest that any illness, however minor, could be related to the infections produced by the administration or spread of the vaccine virus strains.

Comment

Although the primary object of this still-continuing investigation was the study of the transmission of infection with the attenuated poliovirus vaccine strains of Sabin, the results relative to primary infection in the vaccine recipient are of interest. With oral inocula consisting of approximately 100,000 infectious units, the dose recommended by Sabin for routine use, all of the three strains considered were able to initiate infection in all but one of the presumably susceptible persons. However, pharyngeal infection after administration of doses of this size was exceptional, in contrast to the usual appearance of virus in the throat after a larger inoculum containing somewhat more than 10 million viral particles. A dose of 4,000 units of type 1 virus failed to infect four persons to whom it was given, and an equal dose may have been on the border line of infectivity with type 3. All of the foregoing suggests that the infectivity of the attenuated strains must be considerably less than that of "wild" strains. This is consistent, moreover, with the greatly reduced intrafamilial dissemination of the attenuated strains, as compared with the results of studies of natural poliovirus infections with the same and similar families [11] in which more than 90% of susceptible persons became infected.

After infection in the recipient, however, the sequence of events, in terms of the duration of pharyngeal and fecal excretion of virus and of serologic response, greatly resembles that which follows natural infection in Salk-vaccinated persons. Unfortunately, titrations of virus in fecal extracts have not yet been made. The failure of many persons to manifest an antibody rise, especially if the preinfection titer derived from formalinized vaccine is greater than 1:40, should be re-emphasized, since this phenomenon renders invalid studies based exclusively on serologic examination. The rise in antibody titer, when it did occur, between the 7th and 10th day after ingestion in the majority of persons,

Table 8.—*Examples of Families Experiencing Episodes of Natural "Wild" Enterovirus Infections* Coincident with Administration of "Sabin Vaccine"*

Family Status	Age, Yr.	Natural Immunity Status†	Presence of Virus in Feces on Day							
Unit 10: Upper Economic, Index Fed 5.3 Log Dose Type 1										
			0	1	2	4	7	9	14	21
Father	...	I	—		—	—	—		—	—
Mother	...	I	—		B5	B5	B5	B5		B5
Children	8	S	B5	B5		B5	B5	B5	B5	
→	5	S	B5	B5	1	1	1	1		1
	2	S	B5		B5	B5		B5	B5	B5
Unit 15: Negro, Index Fed 7.3 Log Dose Type 1										
			0	2	3	6	12	20	38	55
Father	...	I	—		—	—				
Mother	...	I	—		—	2	—	—	—	
Children	6	S	2		2	2	—	—	—	
	5	S	—		2	2	2	—	—	
	4	S	2		2	2	2	—	—	
→	2	S	—	1	1	1	1	1	—	2
Unit 46: Caucasian-Lower Economic, Index Fed 7.1 Log Dose Type 3										
			0	2	4	5	7	8	10	26
Father	...	I	—	—	—	—	—	—	—	
Mother	...	I	—	—	—	3	—	—	—	
Children	18	I	—	—	—	—	—		—	
	13	I	—	—	—		—	—	—	
	12	S	—	—	—		3		—	3
	10	S	—		E1+3		—	3	—	3
	8	S	E1	E1	E1	3	E1	3	—	3
	5	S	—		E1	—	—	E1	3	3
→	4	S	—	3	3	3	3	3		3
	1	S	E1	E1	E1	—	E1		3	3

* Natural "wild" Enteroviruses: Coxsackie B5, ECHO 1, and poliovirus type 2. Fed "index" child indicated by arrow.

† With reference to vaccine virus type fed. I=immune; S=susceptible.

does not suggest that the previous sensitization with Salk vaccine had produced an accelerated response, although comparable studies in unvaccinated persons were not done.

Among the 46 family units in which spread of virus from a vaccine-induced infection was studied, the more readily identifiable variables were virus type, virus dose, and the related pharyngeal excretion of virus, socioeconomic status, and age of the index person. Perhaps of at least equal importance in influencing viral transmission are concurrent infections with other enteric viruses and subtle variations in the interpersonal relationships of the individuals comprising these families. Because of the multiplicity of variables and the small numbers of units per identified variable, conclusions as to the influence of individual factors in predisposing to or limiting transmission seem justified only if the results are definite and consistent.

Among the three virus types, there is a suggestion that type 3 ordinarily may spread more readily than either of the others; however, in individual instances, both types 1 and 2 viruses infected all of the contacts. A direct effect of virus dose was not noted, but the larger (7 log) doses resulted in a greater proportion of index pharyngeal excretors, who in turn were associated with more extensive transmission of types 2 and 3. However, the significance of this is weakened by the fact that development of infection of some contacts appeared well after pharyngeal excretion had ceased. Since fecal extracts have not yet been titrated, some association between virus titer in the feces and viral multiplication in the throat cannot be ruled out. Moreover, a possible effect of the larger dose on suppressing or aborting coincidental "wild" virus infections has not been evaluated. Nonetheless, although pharyngeal excretion may have some effect in increasing the probability of virus transmission, the demonstration that spread occurs readily in its absence is of much greater import. This relates to the suggestion by Salk [12] that, if formalinized vaccine reduces pharyngeal multiplication, and if the transmission of poliovirus is by way of pharyngeal excretions in a well-sanitated population, then the widespread use of a formalinized vaccine may reduce the volume of transmission in such a community. Spread certainly did occur in many of these Salk-vaccinated families in the demonstrated absence of pharyngeal excretion of virus. Furthermore, spread of infection did not occur among several families from the upper economic group in which the index person was a mother who was excreting virus from the throat.

The one variable which definitely played a role in controlling the extent of intrafamilial transmission was socioeconomic status. Only 9% of susceptible contacts from the upper economic group became infected as contrasted with 53% among households from the lower economic group. This is a much greater difference than was seen in episodes of natural poliovirus transmission where the infection of almost all susceptible contacts is the rule, regardless of sanitary status. This probably is to be explained by the lesser infectivity of the attenuated strains.

The demonstration of transmission of vaccine viruses outside the family unit to play contacts suggests the possibility that an entire community might be saturated with these strains, if they were administered to a sufficiently large proportion of the susceptible children present. Despite their lower infectivity, the multiple opportunities for contact then available might enable them to compete effectively with other, "wild" strains present in the population, eventually, perhaps, to displace them.

Interference between enteroviruses has been demonstrated often in the laboratory, and has been postulated as an explanation for some peculiarities in the occurrence of epidemics of poliomyelitis and pleurodynia.[13] If this is a phenomenon which occurs under natural conditions, we might expect that the introduction of a related enteric virus into a household coincidentally with the administration of an attenuated strain might inhibit the spread of the latter, as is strongly suggested in certain of our unit studies. Thus, while, in practice, extensive community spread of vaccine polioviruses may be limited in good environments by superior hygienic standards, it may, rather paradoxically, be limited by viral interference in poor environments. If such interference takes place commonly, it might be of great importance in limiting the effectiveness of mass live-virus immunization programs in poorly sanitated areas.

Finally, the total absence during this study of harmful effects consequent to infection with these living, attenuated poliovirus strains is to be noted. Although the persons taking part were few in number, these results may be added to the rapidly growing record of safety which is being accumulated for this method of immunization against poliomyelitis.[9]

Summary

A study of the spread of infection with Sabin's living, attenuated strains of polioviruses was conducted in 56 "Salk-vaccinated" household units in New Orleans. Each unit contained at least three naturally susceptible members, one of whom was fed the oral vaccine. The course of infection in this index person was followed by virologic and serologic means, and spread to other persons within and without the families was similarly studied. The effect of such variables as virus type, virus dose and the related excretion of virus in the pharynx, socioeconomic status, and age of the vaccine recipient was investigated. All except one adult became infected after the feeding of at least 100,000 infectious units, and transmission to many contacts was detected. Socioeconomic status appeared to have the most marked effect on spread, upper status usually

being associated with failure of transmission. Interference to spread of the attenuated strains by other, "wild" enteric virus infections among families from the lower economic group was strongly suggested. No illness was associated with either primary vaccine administration or contact infection.

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HUMAN PHARMACOLOGY OF THIAZIDE DERIVATIVES

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Chlorothiazide in doses of 1 Gm. by mouth twice daily induced the excretion of practically the same amounts of sodium and chloride as did 2 cc. of a molar solution of meralluride injected intravenously. When the chlorothiazide was administered daily for two or three weeks, the sodium excretion declined until it approached the daily intake, and the patient's body weight approached a steady level about 4 lb. (1.8 kg.) below the initial level. A nearly maximal rate of sodium excretion was obtained with 2 Gm. of either chlorothiazide or flumethiazide, and increasing the doses to 4 Gm. did not yield further significant increases of sodium excretion. For hydrochlorothiazide the dose required to give maximum excretion rates was 200 mg. A steadier effect and over-all increase in response resulted from giving doses of 200 mg. of hydrochlorothiazide every 12 hours as compared to 400 mg. given once a day.

Numerous clinical conditions of diverse etiology are associated with sodium and water retention, due usually to increased reabsorption by the renal tubules. Because of the varied causes of edema, a drug, if it is to be effective, must be adequately potent to depress the reabsorption of sodium and water irrespective of the etiology of the retention.

Chlorothiazide (Diuril) is an effective natruretic and diuretic agent when administered orally, and it compares favorably with the organomercurials which are given parenterally. As in the case of the organomercurials, the increase in water excretion is secondary to the natruresis. Although the incidence of serious side-effects after the administration of chlorothiazide is low, a number of derivatives of chlorothiazide have been developed in an effort to find more potent compounds with fewer side-effects. This report presents certain pharmacological properties of chlorothiazide and two of its derivatives,

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flumethiazide (Ademol) and hydrochlorothiazide (Hydrodiuril), placing particular emphasis on the response in electrolyte excretion.

Effect on Electrolyte Excretion

Chlorothiazide inhibits carbonic anhydrase in vitro, being more active than sulfanilamide but less active than acetazolamide (Diamox).[1] In vitro, chlorothiazide exerts its effect primarily in the renal tubules. Some investigators[2] propose that chlorothiazide produces its diuretic response by inhibition of sodium and chloride reabsorption, with subsequent exchange of some of the sodium for potassium in a more distal portion of the tubule, resulting in a moderate increase in potassium excretion. These authors also compared chlorothiazide and meralluride (Mercuhydrin). They concluded that chlorothiazide acts more distally in the renal tubule than meralluride. Presumably flumethiazide and hydrochlorothiazide have the same action.

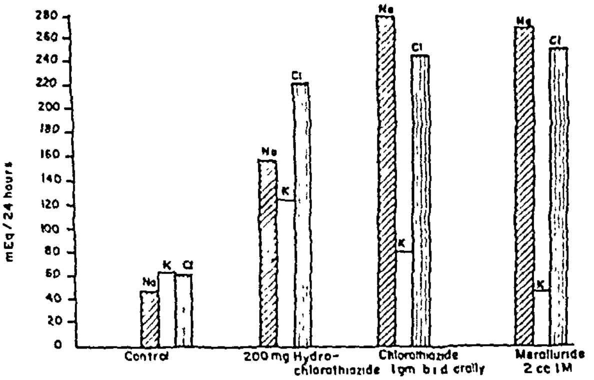

Fig. 1.—Effect on sodium, potassium, and chloride excretion of hydrochlorothiazide as compared to chlorothiazide and meralluride.

Chlorothiazide and the two derivatives (hydrochlorothiazide and flumethiazide) produce effects within 2 hours after oral dosage that reach a maximum within 6 hours; the response persists for 12 hours or more. The primary effect of chlorothiazide is an increase in sodium excretion, with a slightly lesser effect on chloride excretion (fig. 1). There is a moderate and consistent increase in potassium excretion. As a compensatory renal mechanism to conserve sodium, ammonia excretion is increased during the second 12-hour period but shows no increase before that. The increase in the rate of excretion of bicarbonate is about one-fourth that of chloride. Phosphate excretion is not altered. By contrast, a carbonic anhydrase inhibitor such as acetazolamide produces an immediate augmentation of sodium excretion, with an almost equal effect on potassium and bicarbonate excretion. Acetazolamide suppresses chloride excretion during the period of greatest bicarbonate loss, but the former increases when the latter subsides. Phosphate excretion is not affected by carbonic anhydrase inhibitors.

In general, the spectrum of activity of chlorothiazide appears to resemble that of the mercurial agents. As with administration of the thiazide derivatives, the administration of meralluride parenterally is followed by an onset of action within one hour which reaches its maximum in 2 to 6 hours, and the natruretic effect lasts for 12 to 18 hours. An increased excretion of sodium and chloride is the predominant effect,[3] while potassium excretion is not significantly altered (fig. 1). Ammonia excretion, slightly depressed at first, becomes elevated after the period of greatest sodium loss. During the stage of greatest chloride loss, bicarbonate excretion is suppressed, but this returns to normal or higher when the chloruretic response subsides.

The predominant effect of chlorothiazide and flumethiazide is to increase sodium excretion, with a lesser but nearly equal effect on chloride excretion. By contrast, the predominant effect of hydrochlorothiazide is to increase chloride excretion, with a lesser effect on sodium (fig. 1).

Ford[4] compared the response to chlorothiazide given alone and in combination with meralluride or the carbonic anhydrase inhibitor acetazolamide. With the former combination, the response was additive. With the latter combination, the maximum chloride output was only one-half that of sodium and the bicarbonate loss was fourfold to sixfold greater than that which occurred when chlorothiazide alone was given.[4] There was a modest increase in sodium excretion. It appears from both preclinical and clinical studies that the effects of chlorothiazide on sodium excretion are additive to those of mercurial diuretics as well as to the response to carbonic anhydrase inhibitors. It is quite possible that chlorothiazide shares a common mechanism of action with meralluride and another with acetazolamide but that it also acts through a third, noncompetitive mechanism.[5]

Both meralluride and the thiazide derivatives reverse the effects of vasopressin (Pitressin), which normally decreases urine flow but does not alter the rate of electrolyte excretion. When chlorothiazide or meralluride is given to dogs who have previously received vasopressin, the urine flow is increased and sodium, potassium, and chloride excretion rates are greatly increased also. The urine is hypertonic with respect to both sodium and chloride, suggesting that the effect is at least partly attributable to a direct influence of chlorothiazide on renal tubular electrolyte transport.

Chlorothiazide also reverses the inhibitory effect of various steroids on salt excretion. When cortisone, hydrocortisone, or fludrocortisone is given to adrenalectomized dogs, sodium excretion is suppressed and potassium excretion is augmented; consequently, the sodium-potassium ratio declines. When chlorothiazide is given at this stage, the sodium excretion increases considerably, with an accompanying small increase in potassium excretion. The relatively greater increase in sodium output tends to raise the sodium-potassium ratio toward normal. Similar observations have been made on patients who were receiving steroids therapeutically.

With continuous daily administration, chlorothiazide has repetitive action (fig. 2). Increased sodium excretion continues until body stores of sodium have been reduced (fig. 2). Serum concentrations of chloride and potassium are slightly depressed, while that of bicarbonate is slightly elevated. The natruretic effect of mercurials is qualitatively similar to that of chlorothiazide. The trend toward hypochloremic alkalosis is sometimes observed with the administration of thiazide derivatives, especially hydrochlorothiazide.

Observations on Renal Hemodynamics

Doses of 0.5 mg. and 10 mg. of chlorothiazide per kilogram of body weight given intravenously appeared not to have a significant effect on mean blood pressure. Glomerular filtration rate was not affected by the 0.5-mg. dose, but after the 10-mg. dose it was slightly depressed, probably as a response to the water and sodium loss (dehydration phenomenon) associated with the diuresis.[3a] It is not likely that chlorothiazide inhibits the renal tubular extraction of para-aminohippurate, since para-aminohippurate clearance was not reduced at the time that chlorothiazide exhibited its maximum effect. In conclusion, the diuretic response to chlorothiazide cannot be attributed to an increase in glomerular filtration rate, indicating that the diuretic response results from blockade of water and electrolyte reabsorption in the renal tubules.

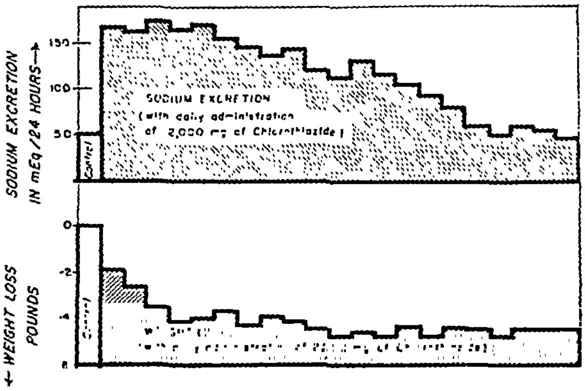

Fig. 2.—Effect of continuous administration of chlorothiazide on sodium excretion and weight loss in patient with minimal edema. After two to three weeks' daily therapy, sodium excretion approximates intake. This occurs as the body stores become depleted. Despite this approximation, weight loss is maintained.

Similar observations have been made on flumethiazide. When 800 mg. of flumethiazide was given orally to patients in heart failure, there was a sharp increase in sodium excretion one hour after the drug was given (fig. 3), and this persisted throughout the period of observation (five hours). There was no effect on mean blood pressure, glomerular filtration rate (fig. 4), or renal plasma flow. Despite the marked natruresis, plasma sodium and potassium concentrations were not altered.

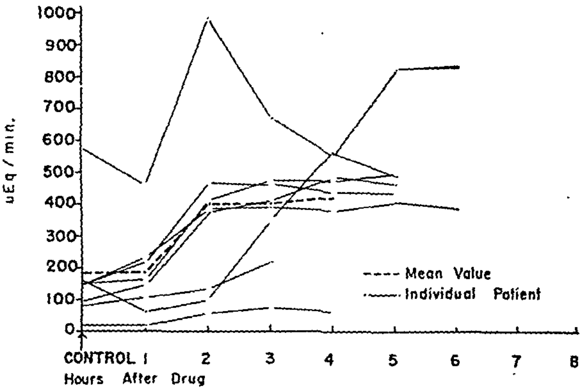

Fig. 3.—Effect of flumethiazide on sodium excretion after single dose of 800 mg. given orally.

Observations on hydrochlorothiazide likewise showed no significant alteration in renal hemodynamics after the administration of 100 mg. orally. When 200 mg. was given intravenously, there was a temporary reduction in glomerular filtration rate which returned to control levels within one hour after the drug was given.

Bioassay Studies

Dose response curves, with sodium excretion used as the critical modality, were determined for patients who were on a controlled sodium intake. Since the patients were in electrolyte balance on a diet containing 50 mEq. of sodium, the control excretion in the urine was approximately 90% of the dietary sodium (about 45 mEq.). The average increase in the 24-hour urinary sodium excretion after chlorothiazide was 44 mEq. after the 500-mg.

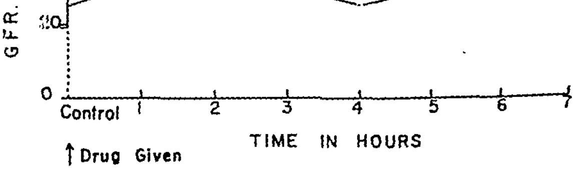

Fig. 4.—Effect of single 800-mg. oral dose of flumethiazide on glomerular filtration rate. Lines indicate responses of individual patients. There was no evidence of significant increase or reduction in glomerular filtration rate within six hours after administration.

dose and 104 mEq. after the 2,000-mg. dose (fig. 5). There was no additional natruresis when the dose was increased above 4 Gm. and very little increase when the dose was increased from 2 to 4 Gm. (fig. 5). Similar observations were made when flumethiazide was administered (fig. 6). The curve of response to hydrochlorothiazide is shifted to the left. A significant increase in sodium excretion starts at the 25-mg. dose and increases to a maximum at the 200-mg. dose level (fig. 7). This appears to be the maximum effective dose level, and no further increase in sodium excretion is produced by a dose larger than 200 mg. The chloruretic response was noticeably larger than the natruretic response, and potassium excretion was approximately one-half that of sodium. At maximum responses for chlorothiazide and hydrochlorothiazide, the increase in sodium excretion was the same, although the dose required to produce this maximum effect with hydrochlorothiazide was only about 10% of that required with chlorothiazide.

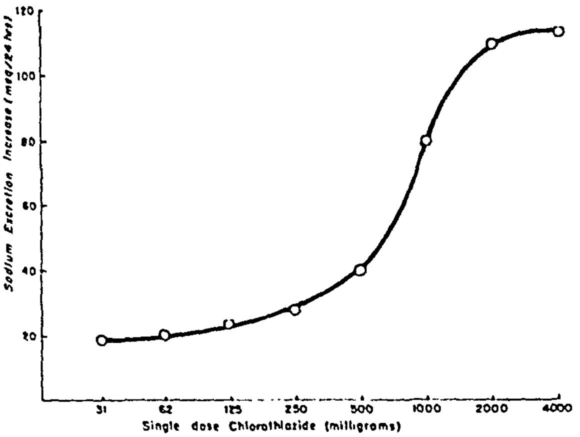

Fig. 5.—Curve of response to chlorothiazide, with increase in sodium excretion used as reference point. Minimal effective dose appeared to be between 125 and 250 mg. Dose which produced maximum increase in excretion was about 2,000 mg. Increase was not significant when dose was increased from 2,000 to 4,000 mg. (Reproduced from Ford and others: A. M. A. *Arch. Int. Med.* **100:**582 [Oct.] 1957.)

When potency of chlorothiazide is compared with that of other diuretics, it appears that a dose of meralluride (1 cc.) equivalent to 40 mg. of mercury produces an increase in sodium excretion that is equivalent to about 1,000 mg. of chlorothiazide administered orally, and 700 mg. of chlorothiazide is equivalent to 1 cc. of mercaptomerin (Thiomerin) administered parenterally. When both drugs are administered orally, four tablets (equivalent to 40 mg. of mercury) of chlormerodrin (Neohydrin) are equivalent in natruretic potency to 560 mg. of chlorothiazide. The response to flumethiazide is about the same at equal doses. The response to hydrochlorothiazide is also about the same, but at 10% of the dose of chlorothiazide.

To determine differences in sodium and potassium excretion for chlorothiazide given as a single dose and as fractional doses per 24 hours, the sodium and potassium excretion was observed in a patient who received 4,000 mg. as a single dose at 6 a. m. After a suitable recovery period (seven days) the drug was given as 1,000 mg. every six hours for four doses. There was a greater potassium loss on the fractional dose schedule. However, there was an even greater sodium loss, indicating the advantage of fractional doses. Similar observations have been made with flumethiazide and hydrochlorothiazide (fig. 8).

Nervous System Effects

Chlorothiazide appears to be free of actions on the nervous system. Consequently, it does not have appreciable antiepileptic, anesthetic, analgesic, or antiglaucomatous effects. Unlike acetazolamide, it apparently does not penetrate the blood-brain barrier and is consequently not distributed through the central nervous system in appreciable concentration. For this reason it produces little effect referable to the central nervous system.

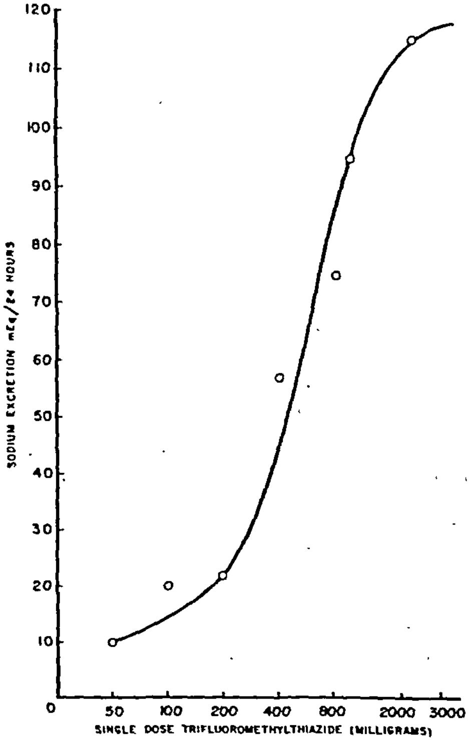

Fig. 6.—Curve of response to flumethiazide (trifluoromethylthiazide). Curve is similar to that observed after administration of chlorothiazide (fig. 5).

Evidence indicates that chlorothiazide, even in large intravenous doses, has no significant effect on the cardiovascular-respiratory system of anesthetized dogs. Cardiovascular effects of injected acetylcholine, histamine, epinephrine, and nicotine were unaltered by chlorothiazide, as was the reflex pressor effect of central vagal stimulation. No effect was noted on mean arterial blood pressure or heart rate. These findings indicate that the drug does not possess significant antihistaminic, adrenergic-blocking, atropine-like, or ganglionic-blocking activity.

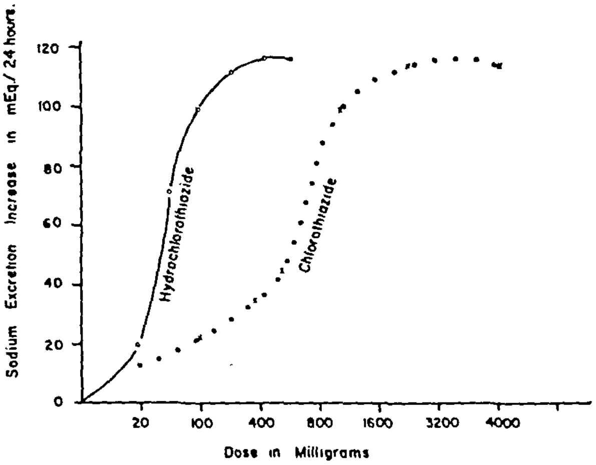

Fig. 7.—Dose-response curve for hydrochlorothiazide as compared to chlorothiazide. Curves were similar but with smaller dose of hydrochlorothiazide. However, greater increase in sodium excretion could not be obtained by its administration. Maximum effective dose of hydrochlorothiazide appeared to be about 200 mg. and that of chlorothiazide was about 2,000 mg.

Clinical Use

The initial dosage of chlorothiazide and flumethiazide in edematous subjects is 1 to 2 Gm. daily, and for hydrochlorothiazide it is 100 to 200 mg. daily for three to five days or until overt edema disappears. This is followed by administration of a maintenance dose of 250 mg. to 1.0 Gm. of chlorothiazide and flumethiazide and 25 to 100 mg. of hydrochlorothiazide daily. Total daily amounts of over 500 mg. of chlorothiazide and flumethiazide and 50 mg. of hydrochlorothiazide are customarily given in two divided doses at 8-to-12-hour intervals. Since these compounds exhibit a rising dose-response curve,[3b] the dosage should be adjusted to the needs of the patient. Therapy in severely ill patients is started at higher dosage levels than in those with moderate or mild edema. The dosage and frequency of administration should be readjusted subsequently according to the patient's response.

In mild or moderate edema, smaller doses and intermittent administration, for two or three days per week, may be preferable. Occasionally even severely ill patients will respond better to intermittent administration (three days per week).

For premenstrual tension, therapy with 500 mg. of chlorothiazide or flumethiazide or 50 mg. of hydrochlorothiazide daily is usually started five to seven days before the period and discontinued at the onset of menses. In edema of pregnancy, with or without hypertensive vascular disease, similar daily doses for five days per week are recommended. Lower doses have failed to produce sufficient initial diuresis.

When the thiazide derivatives are first administered to hypertensive patients being treated with other drugs, it is advisable to continue giving Rauwolfia derivatives in the standard dosage and to reduce the dose of the other agents (fig. 9). The dose particularly of the ganglionic-blocking agents should be reduced one-half or more (to avoid a possible precipitous fall in blood pressure), and then it should be increased or decreased in small increments according to the patient's response. Careful, repeated observations of blood pressure, *especially during initial therapy*, are essential. Doses of chlorothiazide and of other antihypertensive drugs given simultaneously can sometimes be further decreased, once the blood pressure becomes stabilized at the lower level.

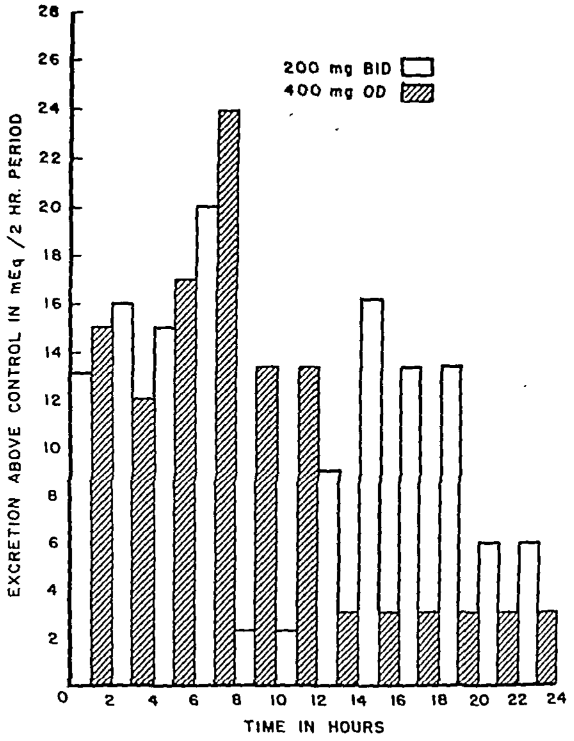

Fig. 8.—Natruretic response to hydrochlorothiazide, 200 mg. every 12 hours as compared to 400 mg. given once a day. Although there was somewhat larger response initially to 400-mg. dose, significant increase in excretion occurred when second 200 mg. was given in twice-a-day regimen.

Therapeutic Precautions

Edema syndromes, particularly heart failure, may be associated with electrolyte abnormalities. Some of these are due to coexistent gastrointestinal, hepatic, renal, or pulmonary disturbances, while others may be the result of intensive or excessive use of therapeutic agents. These electrolyte disturbances may cause serious symptoms and may also render the underlying disease unresponsive to therapeutic regimens. An electrolyte imbalance should be suspected (and confirmed by chemical studies) in all patients whose conditions become refractory to diuretic agents. However, when careful appraisal shows that both symptoms and electrolyte disturbances arise from progression of the underlying disease, diuretic therapy will probably be of no avail. Electrolyte disturbances caused by vigorous diuretic therapy, on the other hand, can usually be readily corrected.

Hypochloremic alkalosis may be avoided by a judicious adjustment of the dosage and frequency of administration of thiazide derivatives and by avoidance of rigid salt restriction. This side-effect is most likely to occur in association with the administration of hydrochlorothiazide, since the primary effect of this agent is to increase chloride excretion rather than sodium excretion. This response is in contrast to that with the other thiazide derivatives. Temporary cessation of drug therapy or the administration of ammonium chloride prevents or corrects the alkalosis if it does occur. The therapist should remember that, in patients with hepatic insufficiency, ammonium salts can produce ammonium intoxication. The low-salt syndrome as a complication of therapy with the thiazide compounds does occur occasionally. When the history and blood electrolyte studies establish the fact that sodium depletion is present, salt can be given by mouth or a cautious infusion of hypertonic sodium chloride may be used. Water should rigidly be restricted while the infusion is being given and for three to six hours thereafter. Diuretic therapy is usually discontinued until the reestablishment of a normal or nearly normal blood electrolyte pattern.

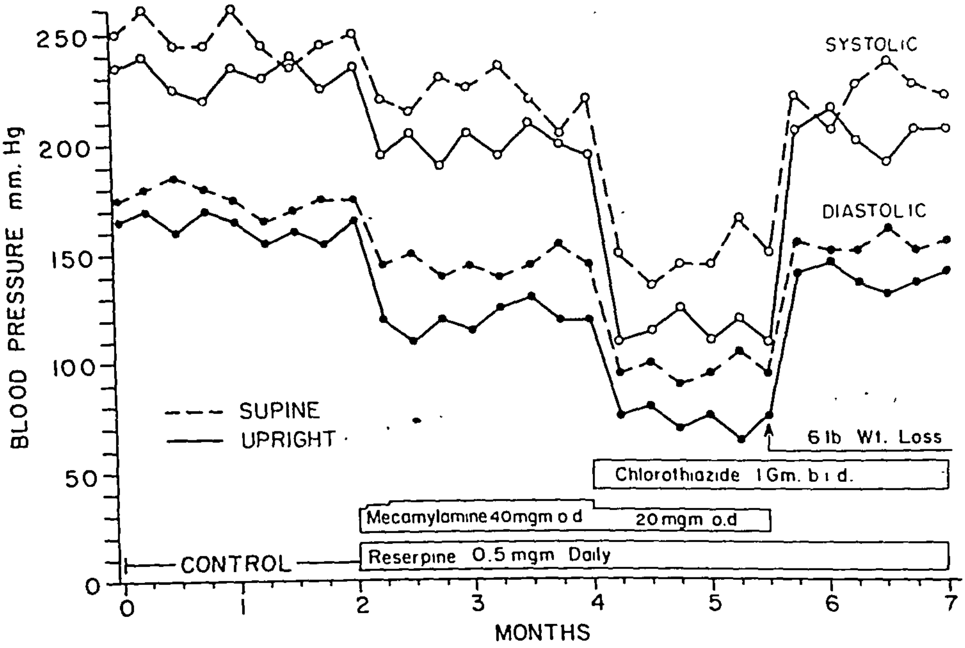

Fig. 9.—Effect of chlorothiazide on blood pressure response to rauwolfia and ganglionic-blocking agent in hypertensive patient with left ventricular strain. Even with one-half the original dose of blocking agent, reduction in blood pressure was much greater than that observed while patient was taking rauwolfia and mecamylamine without diuretic. (Reproduced with permission from *Ann. New York Acad. Sc.* **71**:456, 1958.)

Intensive or prolonged administration of chlorothiazide and its derivatives may produce hypokalemia. Mild depression of serum potassium level usually produces no symptoms. As the potassium deficit accumulates, gradual diminution of strength is noted; the muscles tend to become flaccid and the reflexes, hypoactive or absent. The patient may complain of weakness only, or of numbness of the extremities. When the hypokalemia is severe, symptoms include apathy, drowsiness, anorexia, nausea, paralytic ileus, hypotension, and shallow, infrequent respiration. Hydrochlorothiazide is more likely to produce potassium depletion (hypokalemia) than are chlorothiazide and flumethiazide.

Significant electrocardiographic changes may appear when the serum potassium level drops to 3 mEq. per liter or lower. These are prolongation of Q-T interval due mainly to flattening and widening of the T wave, T-wave inversion, and depression (sagging) and low "take-off" of the S-T segment. These changes may occur independently or in combination.

Hypopotassemia sensitizes the myocardium to the action of digitalis and may result in digitalis toxicity. This is indicated by cardiac arrhythmias, most often paroxysmal auricular tachycardia with block. Treatment consists of omitting digitalis and administering potassium, preferably orally, care being taken not to bring on potassium intoxication.

Prophylactic administration of potassium chloride or citrate (1 to 6 Gm. daily) along with chlorothiazide is particularly recommended in patients with conditions which may be associated with potassium deficiency, especially with fever or when excessive loss (with diarrhea) is imminent. Potassium deficiency may also develop during the administration of some adrenocortical steroids.

Conclusions

In the final analysis, diuretic therapy is only one important facet of the management of edematous patients. An effort must always be made to correct the underlying abnormality when specific therapy is available.

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ACUTE PANCREATITIS IN PATIENTS RECEIVING CHLOROTHIAZIDE

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and

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Acute pancreatitis was diagnosed in three women, all 50 years of age or older, who had been taking 0.5 to 1.0 Gm. of chlorothiazide daily for two or three months in the course of treatment for cardiovascular disease. In no case was there a history of conditions usually considered as predisposing to acute pancreatitis. The diagnosis was based on both clinical and laboratory studies and was confirmed in one case by histological study of autopsy material. Although the specific etiology remained undetermined, chlorothiazide was considered as a possible cause. The authors wish to alert physicians to this possibility, which may warrant further investigation.

Chlorothiazide, since its introduction in 1958, has gained widespread acceptance as an effective and relatively safe diuretic and antihypertensive agent. Undesirable effects occurring after the use of chlorothiazide have been largely those resulting from electrolyte disturbances. These disturbances actually reflect exaggerated therapeutic responses and are not true reactions of toxicity. However, there have been scattered reports of direct toxic effects, such as papular skin rashes,[1] exfoliative dermatitis,[2] purpura,[3] and jaundice.[4] In our experience, as well as that of others, such toxic effects are extremely rare; however, within the past year we have observed the development of severe acute pancreatitis in three patients who had been taking chlorothiazide daily for several months. These patients did not have any of the usual precipitating causes of acute pancreatitis, such as associated cholecystic disease, pancreatic tumor or infection, injury to the pancreas, or alcoholism. It seems timely, therefore, to call to the attention of others the possibility that pancreatitis may be a complication of chlorothiazide therapy. A report of these three cases follows.

Report of Cases

CASE 1.—The patient was a 78-year-old widow who had severe arteriosclerotic heart disease. Control of her symptoms of congestive heart failure had required salt restriction, digitalis therapy, and injections of meralluride three times per week. On Jan. 7, 1958, the meralluride therapy was discontinued and the administration of 1 Gm. of chlorothiazide daily was begun. The digitalis therapy was continued, but no other medicaments were given. Satisfactory control of the congestive heart failure ensued and the patient noted that taking the chlorothiazide daily freed her from the "ups and downs" of intermittent mercurial diuresis.

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At 4 a. m. on April 1, 1958, she was awakened by severe abdominal pain and repeated vomiting. She was seen shortly thereafter at home. Physical examination revealed an acutely ill, cyanotic, elderly female in severe distress. The skin was cold and moist. The cardiac sounds were of fair quality, the rate was 72 beats per minute, and the rhythm was completely irregular. The lungs were free of rales. The abdomen was distended and silent; tenderness was present in the epigastrium and right upper quadrant. Results of rectal and pelvic examinations were negative. The peripheral pulsations were intact.

The patient was admitted to the hospital later that morning. Laboratory studies done about seven hours after the onset of her pain revealed an erythrocyte count of 4,930,000 and leukocyte count of 21,000 per cubic millimeter of blood, with 87% neutrophils, of which 11% were band forms. The concentration of hemoglobin was 14.2 Gm. per 100 cc. of blood. Results of urinalysis were negative. The serum amylase level was 1,630 units per 100 cc. A plain roentgenogram of the abdomen revealed a few gas-containing loops of small intestine but no free air or abnormal calcifications.

The diagnosis of pancreatitis was obvious, and the patient was treated with sedation, administration of atropine, nasogastric suction, and fluid replacement. On the third hospital day the serum amylase level was 562 units per 100 cc. However, the patient's condition steadily worsened, and 75 hours after the onset of abdominal pain she died. Postmortem examination revealed severe hemorrhagic pancreatitis with widespread fat necrosis. The liver, gallbladder, and bile ducts were normal.

Case 2.—The patient was a 52-year-old married female who had had moderately severe hypertensive vascular disease for several years. Two years previously she had had an acute cerebrovascular accident resulting in a spastic right-sided hemiparesis. Her blood pressure had ranged from 190 to 250 mm. Hg systolic and from 118 to 120 mm. Hg diastolic. On July 14, 1958, her blood pressure was 210 mm. Hg systolic and 130 mm. Hg diastolic. At that time the administration of 5 mg. of mecamylamine and 500 mg. of chlorothiazide daily was begun.

On Nov. 6, 1958, the patient was admitted to the hospital because of severe abdominal pain, nausea, vomiting, weakness, and polyuria. Physical examination revealed a confused, drowsy, dehydrated, obese woman. Her blood pressure was 190 mm. Hg systolic and 115 mm. Hg diastolic. The cardiac rate was regular and the heart was of normal size, but there was a grade 1 systolic apical murmur. Examination of the ocular fundi revealed grade 2 hypertensive changes. Dental caries and marked periodontoclasia (pyorrhea alveolaris) were present. The abdomen was distended, tender, and silent. The concentration of hemoglobin was 16.6 Gm. per 100 cc. of blood. The erythrocyte count was 6,100,000 and the leukocyte count 10,800 per cubic millimeter of blood, with 87% segmented neutrophils, 5% band neutrophils, 7% lymphocytes, and 1% monocytes. The sedimentation rate was 49 mm. in one hour (Westergren method). Urinalysis revealed a specific gravity of 1.028, glycosuria (4+) and acetonuria (2+). Results of microscopic examination of the urine were negative. The blood glucose level was 1,200 mg.%. The serum amylase level was 700 units per 100 cc. (corrected for the high glucose level in the blood). The cerebrospinal fluid was normal. The blood urea nitrogen level was 100.8 mg.%.

On the second hospital day the patient developed shock, her temperature rose to 104 F (40 C), and she became comatose. A constant intravenous infusion of arterenol was required to sustain her blood pressure level. However, with the help of intravenous administration of fluids, maintenance of constant gastric suction, and administration of anticholinergic drugs and insulin, she slowly regained consciousness, her abdominal pain disappeared, and her blood urea nitrogen and fasting blood sugar returned to normal levels. The serum amylase level was 280 units per 100 cc. on the 5th hospital day, 365 units on the 8th day, and 50 units on the 12th day. Roentgenograms of the gallbladder and upper part of the gastrointestinal tract taken when the patient became ambulatory were normal. An electrocardiogram revealed a pattern of left ventricular hypertrophy. On the 48th hospital day the patient was transferred to a nursing home for continued supportive care.

She was seen again on Jan. 12, 1959, in the outpatient department of the hospital. Her blood pressure was 200 mm. Hg systolic and 130 mm. Hg diastolic. She felt well and had had no further abdominal pain. Urinalysis revealed no sugar or acetone. The fasting blood sugar level was normal, and the administration of insulin was no longer necessary.

Case 3.—The patient was a 71-year-old widow who had been chronically ill with rheumatic heart disease, mitral insufficiency, and chronic congestive heart failure for about three years. She had been on a low-salt diet and therapy with digitoxin and mercurial diuretics until December, 1958, when the administration of chlorothiazide, 0.5 Gm. daily, was substituted for the mercurial diuretics.

On March 30, 1959, the patient suddenly began to have severe generalized abdominal pain with nausea and vomiting. The pain was steady and only temporarily relieved by administration of meperidine hydrochloride. The patient was, therefore, admitted to the hospital. She had no family history of pancreatitis. She never had consumed alcoholic beverages. Physical examination revealed an acutely ill, nauseated, dyspneic female. The blood pressure was 170 mm. Hg systolic and 100 mm. Hg diastolic. The pulse rate was 80 beats per minute. The respirations were rapid and shallow. Her temperature was 97 F (36.1 C). Examination of the ocular fundi revealed arteriolar sclerosis, grade 2 (according to the classification of Keith, Wagener, and Barker). The heart was enlarged to the left anterior axillary line, with a diffuse, heaving, apical impulse and a grade 4 systolic apical murmur. Auscultation of the lungs revealed a few medium moist rales in both bases. Abdominal examination revealed generalized tenderness, which was most marked in the upper part of the abdomen, accompanied by involuntary muscle spasm and rebound pain. There was moderate gaseous distention, and peristaltic activity was markedly decreased. The peripheral pulses were full and equal, and there was no pitting edema of the ankles or legs. Results of rectal examination were negative. The patient was somewhat confused and irrational. Her lips were cyanotic. The concentration of hemoglobin was 11.9 Gm. per 100 cc. of blood. The leukocyte count was 16,150 per cubic millimeter of blood, with 94% segmented neutrophils. Urinalysis revealed albuminuria (1+) and 2 to 3 white blood cells per high-power field. The serum amylase level was 925 units per 100 cc. A plain roentgenogram of the abdomen revealed a calcified, tortuous aorta but no other abnormality. The roentgenogram of the chest revealed the lung fields to be clear but the heart markedly enlarged. The blood calcium level was 7.5 mg.%.

The diagnosis of acute pancreatitis was made. The patient's severe abdominal pain persisted, and she was treated with constant gastric suction and administration of anticholinergic drugs, sedatives, mercurial diuretics, digitoxin (Crystodigin), penicillin, and streptomycin. Because of cyanosis and respiratory distress, administration of oxygen was necessary during the first week of hospitalization. Over a period of nine days the patient's condition slowly improved. Her abdominal pain disappeared, she became mentally clear and rational, the cyanosis disappeared, the dyspnea markedly improved, and she was able to take a soft diet without difficulty. Roentgenograms of the gallbladder and upper part of the gastrointestinal tract on the 14th hospital day were normal. The serum amylase level just prior to the patient's dismissal was 70 units per 100 cc.

Comment

In the majority of cases of acute pancreatitis, either alcoholism or associated disease of the biliary tract is present. In a statistical review, Paxton and Payne[5] found either associated cholecystic disease or alcoholism in 62% of 307 established cases of acute pancreatitis. In the remaining 38% of the cases the etiology of the disease was unknown. To our knowledge, no drug or chemical other than alcohol has been incriminated as an etiological factor in pancreatitis. However, our observation during the past year of the development of severe acute pancreatitis in three patients who were receiving chlorothiazide leads us to suspect that this may be more than a coincidence. None of these three patients was an alcoholic or had associated biliary tract disease. All were middle-aged or elderly females. All had received chlorothiazide daily for several months. None had developed any untoward digestive symptoms or evidence of gastric irritation. None had a family history of pancreatitis. All had serious vascular disease. The pancreatitis was fatal in one case. The other two patients recovered, after prolonged hospitalization.

Summary and Conclusions

During the past year we have observed the development of acute pancreatitis in three patients (all middle-aged or elderly females) who had been receiving chlorothiazide daily for several months and who did not have associated biliary tract disease, alcoholism, or any other of the conditions usually considered important in the etiology of pancreatitis. By reporting these cases, we hope to draw the attention of others to the possible development of pancreatitis in patients who receive chlorothiazide.

Addendum

Since the submission of this manuscript, we have observed a fourth example of pancreatitis associated with the administration of chlorothiazide. The patient is an 84-year-old man with arteriosclerotic heart disease and chronic congestive heart failure, who had taken 1 Gm. of chlorothiazide once or twice a week for 15 months. He is now in the hospital with typical acute pancreatitis. The initial serum amylase level was 890 units per 100 cc. To date he is not well enough for cholecystography, but he gives no history suggestive of gallbladder disease. He has never used alcoholic beverages.

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CLINICAL THERAPEUTIC EVALUATION OF HYDROCHLOROTHIAZIDE (HYDRODIURIL)

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In most patients treated earlier with chlorothiazide, maintenance of the previous status was obtained with a dose of hydrochlorothiazide one-tenth that of chlorothiazide. An important advantage appears to be absence of complaints of weakness during early weeks of treatment. Intravenous administration of hydrochlorothiazide is convenient and effective therapy. In oral therapy, daily administration is preferred because a more constant level of "compensation" is desirable. Hypertensive patients without clinical congestive failure showed improvement both symptomatically and by fall in blood pressure.

The advent of chlorothiazide initiated a new era in diuretic therapy. Since its evaluation by an unusually large number of investigators, this remarkable compound has become a valuable therapeutic tool for countless practicing physicians. Orally given chlorothiazide is as powerful a diuretic as parenterally given mercury and does not itself become ineffective with continued use.[1] It resembles structurally the carbonic anhydrase inhibitors and pharmacodynamically the organomercurial diuretic drugs. The primary effect appears to be inhibition of renal tubular reabsorption of sodium and chloride, resulting in a secondary increase in water excretion. There appears to be some carbonic anhydrase inhibitory effect on the renal tubules, particularly with the use of larger doses.[2]

Further exploration of the benzothiadiazine chemistry by Novello and Sprague resulted in the synthesis of hydrochlorothiazide (Hydrodiuril), the dihydro derivative of chlorothiazide, having no double bond in the heterocyclic ring. Renal clearance studies show that hydrochlorothiazide is cleared by the kidney at a rate greatly in excess of glomerular filtration, attributable to secretion by the epithelial cells of the renal tubule. Preclinical evaluation with various doses demonstrated that the increase in cation excretion that resulted from increasing the dose of hydrochlorothiazide was completely covered by an equal increase in chloride excretion. In the case of chlorothiazide, however, a portion of the cation was covered by an increased bicarbonate excretion (increase in urine pH). The kaliuretic effect in these experiments was the same for both compounds. These findings may be of significance in assessing the clinical results with these compounds.

Materials and Methods

Case Material.—One hundred eighteen patients were selected for treatment with hydrochlorothiazide, of whom 106 were outpatients. Duration of therapy was approximately four months (18 weeks for 69 patients and 17 weeks for 37 patients). Studies with chlorothiazide had been done previously in the majority of these patients; they were classed with those having edema of marked severity, since poor response to organomercurial therapy was seen prior to the administration of chlorothiazide.[3]

Group A included 83 patients previously treated with chlorothiazide, of whom 9 had Laennec's cirrhosis, 32 hypertensive heart disease, and 42 arteriosclerotic heart disease. In regard to severity of heart disease, 26 patients were in functional class 4 and 48 in class 3 (New York Heart Association classification). Group B included 35 patients not previously treated with chlorothiazide. Twenty-three patients in this group received hydrochlorothiazide orally and 12 received this agent intravenously (LyoHydrodiuril). Those receiving the drug orally included six patients with hypertension (without clinical evidence of congestive failure), one with Laennec's cirrhosis, seven with hypertensive heart disease, and nine with arteriosclerotic heart disease. Those receiving the drug intravenously included two patients with Laennec's cirrhosis, four with hypertensive heart disease, and six with arteriosclerotic heart disease. There were 5 class 4 and 11 class 3 patients among those with cardiac disease who received the drug orally and 3 class 4 and 7 class 3 patients who received it intravenously.

Poor response to organomercurial therapy was a requirement for those patients in group A prior to their original treatment with chlorothiazide; this requirement was not strictly used in the present study for patients in group B, for the practical reason that patients who show poor response to organomercurials and in whom chlorothiazide has not been tried are difficult to find. It is possible, therefore, that the group B patients may not be

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considered as severely ill as were those in group A prior to chlorothiazide therapy; nevertheless, the patients with cardiac failure certainly were among the most edematous of those seen at Kings County Hospital Center.

Thirteen patients with hypertension, who had not previously received chlorothiazide, were given hydrochlorothiazide orally; six of these patients had no clinical evidence of salt and water retention. They are included in this study with the realization that patients with "essential" hypertension may have a slightly elevated serum sodium concentration, expanded total body sodium content, and increased amounts of sodium and water in arterial walls.[4]

Method.—No change in routine was made for the patients in group A (previously treated with chlorothiazide), with the exception of simply substituting hydrochlorothiazide for chlorothiazide. In group B, all diuretic therapy was discontinued, and hydrochlorothiazide was added to the therapeutic regimen. Other than these changes, all measures remained the same and no withdrawal period was used. The patients in this study seldom have been given a low-sodium diet, and they were asked to continue their previous habits—little urging was required. Patients were examined at weekly intervals, and appropriate laboratory studies were done as indicated.

Dosage.—Hydrochlorothiazide was supplied in 25-mg. and 50-mg. compressed tablets and in ampuls containing 50 mg. as powder for reconstitution with distilled water for intravenous use. Patients who had previously received chlorothiazide were given hydrochlorothiazide at one-tenth the dose of chlorothiazide. In group B, those with class 3 cardiac disease were given 50 mg. of hydrochlorothiazide twice daily, as were those with hypertension without overt evidence of congestive failure. Patients with class 4 cardiac disease and those with cirrhosis were given 100 mg. of hydrochlorothiazide twice daily. Patients who received the drug intravenously were given 50 mg. of hydrochlorothiazide in 5 ml. of distilled water once a day; 8 of these 12 patients received two to four such treatments at two-day intervals.

In general, for patients receiving oral therapy, daily administration is preferred in the belief that a more constant level of "compensation" is desirable; this is thought to be one of the main advantages of benzothiadiazine therapy over that with organomercurial agents, which, of necessity, are rarely given daily. To give the benzothiadiazines on an intermittent schedule would eliminate this advantage. From a practical standpoint, the patient is less likely to make mistakes if the habit of administration is a daily one. One dose daily is, of course, ideal if this is sufficient to maintain the desired status; if more than one dose is required, administration at breakfast and at the evening meal is advised, since this approximates 12-hour intervals and eliminates the need for working patients carrying a dose of the drug for midday administration. On this regimen, some patients complain of the necessity of arising at night to urinate, and in these instances administration at breakfast and at lunch is then substituted.

Results

In the majority of the 83 patients previously treated with chlorothiazide, maintenance of the previous status was obtained with a dose of hydrochlorothiazide one-tenth that of chlorothiazide. In approximately one-fourth of these patients, the 10:1 dosage relationship did not hold true, and further adjustment was necessary, with dosage relationships usually resulting in a final ratio of 10:1.5 or 10:2. This minor difficulty offers only temporary inconvenience in changing from chlorothiazide to hydrochlorothiazide therapy. Among the patients who had not previously received chlorothiazide, the original estimated dose requirement was found to be correct for most patients, i. e., 50 mg. of hydrochlorothiazide twice daily for patients with class 3 heart disease and for those with hypertension without overt congestive failure and 100 mg. twice daily for those with class 4 heart disease and for those with cirrhosis. Individual variations were, of course, encountered, and the over-all dosage range is from 25 mg. to 300 mg. daily. One exceptional patient received 450 mg. of hydrochlorothiazide daily and 2 ml. of meralluride three times a week; this patient was formerly receiving 4.5 Gm. of chlorothiazide daily plus the same dose of meralluride. The effective period of action appears to be somewhat shorter for hydrochlorothiazide than for chlorothiazide, and administration three times daily was instituted for approximately one-fifth of patients.

Maintenance of edema-free, compensated status in 83 patients previously treated with chlorothiazide was accomplished with the doses noted above. In 17 patients who had never received chlorothiazide, hydrochlorothiazide produced the same dramatic improvement now familiar with chlorothiazide. Weight and water loss, improvement in the general sense of well-being, diminution or disappearance of edema, and improvement in symptoms were again noted.

No patient in the present study can be classed as showing a therapeutic failure. Only one patient received meralluride; in all other instances control of congestive failure was achieved with digitalis and hydrochlorothiazide, without other adjunctive therapy.

Hypertension.—Patients who had previously received chlorothiazide demonstrated no further change in blood pressure. Patients being treated with antihypertensive agents (usually reserpine) other than chlorothiazide demonstrated a further fall in blood pressure in the order of 20 to 30 mm. Hg systolic and 0-10 mm. Hg diastolic when hydrochlorothiazide was added.

Of six patients with essential hypertension without clinical evidence of congestive heart failure who had never received chlorothiazide and who received no therapy other than hydrochlorothiazide, all demonstrated an improvement in blood pressure and in symptomatology. The range of fall in blood pressure was 50-80 mm. Hg systolic and 10-20 mm. Hg diastolic, usually occurring within the first week of therapy. Postural hypotension was not troublesome symptomatically, though it was occasionally noted on examination. Five of these six patients also had a loss of weight of 3 to 5 lb. (1.3 to 2.3 kg.), which may be considered as water loss. It seems reasonable to suppose that at least a part of the antihypertensive action of hydrochlorothiazide is referrable to improvement of abnormal salt and water metabolism in hypertensive patients presumably free of congestive failure.

Side-effects.—Three patients discontinued hydrochlorothiazide treatment after two to three weeks because of epigastric distress. Two patients developed elevated serum uric acid levels, and one complained of aching knee joints. It has been suggested that these patients have "latent gout" and that the high uric acid levels are due to concentration effects by hydrochlorothiazide in cases of previous decompensation; a more tenable explanation postulates a direct effect on renal tubular metabolism.

No adverse effect on liver function findings or blood cellular constituents was noted. There was no significant change in blood urea nitrogen levels. One patient with Laennec's cirrhosis experienced generalized pruritus and mild diarrhea for two days after the administration of 50 mg. of hydrochlorothiazide intravenously.

Blood Electrolytes.—Changes in serum sodium concentration have been small in degree, inconstantly found, and within normal ranges in all instances. A small drop in serum chloride concentration was common and tended toward reversal by the second week of therapy. There was no significant change in carbon dioxide content.

With chlorothiazide therapy, a significant number of patients complain of weakness during the first one to two weeks of treatment; this symptom disappears usually spontaneously and sometimes with the addition of potassium, either in diet or by tablet. Some instances of proved hypokalemia have been demonstrated. In the present study with hydrochlorothiazide, no evidence of hypokalemia has been demonstrated by serum or electrocardiographic study. No patient was given supplementary potassium chloride or dietary potassium. More significantly, no patient complained of weakness at any time during the study. This finding appears to be the most distinct advantage of hydrochlorothiazide over chlorothiazide.

The lack of weakness with hydrochlorothiazide is certainly a welcome finding, but the explanation remains obscure. Because of the difficulty in proving hypokalemia, it has been supposed that the weakness seen with chlorothiazide therapy was related to low potassium content not demonstrated chemically or electrocardiographically. In a recent series of cases of pregnant women with edema treated with chlorothiazide, approximately two-thirds complained of weakness within the first 48 hours of therapy.[5] It is easy to imagine that pregnancy, with increased amounts of adrenal corticosteroids, might make these patients particularly prone to hypokalemia, but, if this is true, the fact that these women did not respond to supplementary administration of potassium is surprising. Moreover, despite the difficulty in demonstrating low potassium content, a larger percentage of those patients with weakness would be expected to show either serum or electrocardiographic change than has actually been the case. Finally, as has been noted, the kaliuretic effect in animal experiments was the same for both chlorothiazide and hydrochlorothiazide, casting further doubt on the role of potassium in the production of weakness with chlorothiazide or the lack of weakness with hydrochlorothiazide. Whatever the cause, hydrochlorothiazide appears to hold an advantage in this respect.

Intravenous Administration.—Twelve patients received hydrochlorothiazide intravenously, with 50 mg. in 5 ml. of distilled water injected once a day and given again two to four times at two-day intervals in 8 of these 12 patients. Loss of weight 24 hours after administration ranged from 2 to 8 lb. (0.9 to 3.6 kg.), and a reduction of 1+ to 2+ in peripheral edema was noted. Administration by this method is fairly convenient and appears efficacious when parenteral administration is required.

Summary

In 83 patients, hydrochlorothiazide (Hydrodiuril) was substituted for chlorothiazide with relative ease and the edema-free, "compensated" status was maintained with dosages approximately one-tenth those of the latter compound. In 17 patients who had not received chlorothiazide, hydrochlorothiazide produced the same beneficial results as would be expected from chlorothiazide. Hypertensive patients without clinical congestive failure showed improvement both symptomatically and by fall in blood pressure. In patients requiring parenteral administration, intravenous administration of hydrochlorothiazide is convenient and effective therapy. The most important advantage appears to be the lack of weakness in patients receiving hydrochlorothiazide.

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The hydrochlorothiazide used in this study was supplied as Hydrodiuril by Merck Sharp & Dohme, Inc., division of Merck & Company, Inc., Philadelphia.

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HEMORRHAGE FROM MULTIPLE SITES ASSOCIATED WITH CHLORPROMAZINE-INDUCED JAUNDICE

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Hemorrhage occurs rarely during medication with chlorpromazine, and then usually as purpura, without jaundice. Jaundice occurs more commonly; its estimated incidence is 1 to 2%. However, hemorrhage and jaundice can appear together during administration of the drug. A 66-year-old woman had been taking 75 mg. of the drug for 17 days when the yellow color of her skin was first noticed. Three days later she bled spontaneously from the vagina, rectum, and urinary tract, and ecchymotic areas appeared in the skin of the knees. Hypoprothrombinemia due to a toxic action of the drug was considered the cause of the hemorrhage and was corrected promptly by vitamin K_1 therapy; the jaundice secondary to the chlorpromazine-induced hepatitis persisted into the fourth week.

Chlorpromazine, first synthesized in 1951 in France, where it was introduced as an adjunct to anesthesia, has been available in the United States since May, 1954. It has been used for many purposes but mainly to allay neuropsychiatric disorders, to control nausea and vomiting of varied causes, to overcome hiccups, and to diminish intractable pain.

Its side-effects include excessive dryness of the mouth, drowsiness, tachycardia, depression, nasal stuffiness, and a Parkinsonian type of gait and tremor. Distinct from these side-effects are toxic effects, of which the main ones are fever, maculopapular skin eruption, agranulocytosis, and, lastly and probably most important, jaundice.

The incidence of jaundice is difficult to assess accurately. It is approximated as between 1 and 2% when large separately reported [1] series of cases are added together. After five years of its use in the United States, its manufacturer estimated that more than 13 million people had received the drug. Its widespread use continues and the literature is now studded with reports of resulting jaundice and even of cases of liver involvement without clinically detectable jaundice.[2]

With but one exception thus far, no major or minor bleeding has been reported in association with jaundice after use of the drug. The exception is the third of the three cases reported in 1955 by van Ommen and Brown.[3] This patient bled, presumably from a duodenal ulcer. As in most reported cases the prothrombin time was normal.

Among the reports of cases in which there was no jaundice associated with chlorpromazine administration, there are four references to hemorrhagic manifestations. Mullins and associates [4] mention purpuric manifestations among the skin eruptions observed in a series of 85 patients, specifically citing the observation of petechial eruptions in two patients. Platelet counts were normal. Childers [5] reported the development of nonthrombocytopenic purpura in

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two cases. Prothrombin activity was not significantly prolonged (recorded as 78% of normal in one case and 75% in the other). Marley[6] referred to nonthrombocytopenic purpura in one patient who manifested no other bleeding abnormality. Giacobini and Lassenius[7] reported on 147 patients, observing epistaxis in 7, gingival and uterine bleeding in 2, and conjunctival hemorrhage in 2.

Almost without exception, the prothrombin time has been found to be normal or near normal in the patients with hepatitis induced by chlorpromazine.[8] The sole possible exceptions known to us are reports of two jaundiced male patients in whom the respective prothrombin determinations were recorded as 45% and 62% of normal.[9] In neither instance was bleeding described. (Bleeding is ordinarily not encountered even at these levels of prothrombin activity, which generally correspond to times of 16 to 18 seconds.)

Because of the rarity of the occurrence of any bleeding tendency in conjunction with chlorpromazine therapy and its even greater rarity in the presence of jaundice so induced, the following case is reported as an instance of bleeding from numerous sites (skin, rectum, vagina, and urinary tract) in association with jaundice induced by chlorpromazine ingestion. The rectal hemorrhage was massive; the other bleeding was relatively subdued. No cause for the bleeding was elicited other than that associated with the drug-induced jaundice.

Report of a Case

A 66-year-old woman was admitted to Beth Israel Hospital on April 2, 1958, with a chief complaint of yellow color of the skin of three days' duration. The patient had presented herself to the outpatient department on Feb. 5, 1958, with a three-week history of nausea, constipation, and mild abdominal pain. She subsequently attended both the mental health and gastrointestinal clinics. Sigmoidoscopy and roentgenographic examination of the colon showed normal results. Seven weeks prior to admission to the hospital she had been placed on therapy with reserpine and meprobamate with little relief of her symptoms. Three weeks prior to admission the medication was changed to 25 mg. of chlorpromazine, three times daily, by mouth. Three days prior to admission the patient noted the onset of the yellow color of her skin. When this persisted she consulted a local physician who referred her to the hospital.

The patient had not observed the color of her stools but had noted increasingly dark urine with the onset of jaundice. Her appetite was good. There was no history of pruritus, skin eruption, fever, melena, or hematuria. Three days prior to admission she had removed a pessary, worn for uterine prolapse and cystocele. After its removal, she had noted slight bleeding similar to that which had occurred on previous occasions.

The patient had a history of mild hypertension for six years, treated at times with reserpine. A thyroidectomy had been performed 25 years before for hyperthyroidism. The family history and review of systems were essentially noncontributory.

Physical examination revealed a well-developed and well-nourished female in no acute distress but grossly icteric. She was lucid and cooperative. The pulse rate was 80 per minute, blood pressure 150/80 mm. Hg, and temperature 100 F (37.8 C). Marked icterus of both scleras and fundi was observed. No lymph nodes were palpable. The lungs were clear to auscultation and percussion. The heart revealed a grade 2 apical systolic murmur. The abdomen was soft. A smooth nontender liver edge was palpable 3 cm. below the right costal margin. Trophic skin changes and varicosities were evident on the lower extremities. Irregular and macular ecchymotic areas 2 to 3 cm. in size were noted over both knees. Rectal examination showed negative findings. Digital pelvic examination revealed only prolapse and cystocele.

On admission of the patient the hemoglobin level was 13.2 Gm.%, with a hematocrit value of 37%. The white blood cell count was 6,800 per cubic millimeter, with a normal differential count. A catheterized urine specimen revealed a specific gravity of 1.012, with 10 to 15 red blood cells per high-power field and presence of bile (3+) with no increase in urobilinogen.

Several hours after admission the patient passed a few large blood clots from the vagina. Immediate reexamination with speculum by the consultant gynecologist revealed several small bleeding erosions of the vagina at the site of the previously worn pessary. The vagina was packed and the patient appeared comfortable. Twelve hours later (about 2 a. m., April 3, 1958) the patient suddenly had two grossly bloody bowel movements consisting of approximately 700 cc. of dark red blood mixed with clots. Examination at this time demonstrated a blood pressure of 80/60 mm. Hg and a pulse rate of 100 per minute. An infusion of 5% dextrose in water was begun. Before any blood replacement was started the pressure rose to 130/70 mm. Hg. Because of the multiple bleeding sites (skin, vaginal, urinary, and rectal) the possibility of prothrombin deficiency was considered. An emergency blood specimen was taken at this hour for prothrombin time determination to be done later that morning. Fifty milligrams of vitamin K_1 oxide was then administered intravenously. (Due to technical reasons this blood specimen drawn on emergency basis for prothrombin time determination was not suitable for evaluation in the morning.) Proctoscopic examination revealed an ulcerated bleeding hemorrhoid, the area around which was packed with absorbable gelatin sponge. No major recurrence of bleeding from any site was observed thereafter, but minor bleeding did continue for several days as evidenced by microscopic hematuria, rectal ooze, and positive tourniquet test.

The hemoglobin level was 9.2 Gm.% on the morning of April 3, 1958, and the hematocrit value was 24%. The prothrombin time (Quick) on a blood specimen drawn at 9 a. m., April 3, 1958, was 14.1 seconds, with a control of 12.8 seconds. The white blood cell count was 7,450 per cubic millimeter, with a normal differential count. The bleeding time was 3 minutes, coagulation time 9 minutes (Lee-White), and clot retraction time one hour. The platelet count was within normal limits. The fasting blood sugar level was 183 mg.%. The serum bilirubin value was 11.9 mg.%, the thymol turbidity 2.1 units, and the cephalin flocculation a trace at 48 hours. The alkaline phosphatase level was 10.7 Bodansky units, the total cholesterol level 290 mg.% and the cholesterol esters 150 mg.%. The serum glutamic oxalacetic transaminase (SGO-T) value was 73 units.

A chest roentgenogram showed a mild scoliosis with slight enlargement of the heart, pleural adhesions, and apical fibrotic changes. Roentgenographic examination of the esophagus, stomach, and small and large intestine was within normal limits. The gallbladder was well visualized with excellent contractility after a fatty meal. An electrocardiogram showed evidence of a left ventricular strain and hypertrophy. A liver biopsy was performed on the 37th hospital day, but insufficient tissue was obtained for diagnosis. Oral glucose tolerance tests performed on the 7th and 39th hospital days demonstrated a distinct diabetic curve.

Except for a low-grade fever, with temperatures to 100.5 F (38 C), attributed to a chronic cystitis secondary to her cystocele, the patient made an uneventful recovery. On the third hospital day the urine was free of red blood cells, and by the end of the first week all vaginal and rectal bleeding had ceased. No blood replacement was necessary. The patient was prescribed a full diet of 325 Gm. of carbohydrate, 120 Gm. of fat, and 150 Gm. of protein daily, which she consumed voraciously almost from the beginning of her hospital period. In addition she was given therapeutic vitamins daily and a tablet of ferroglycine sulfate complex three times daily.

At the end of the patient's first week in the hospital, the hematocrit value had slowly risen to 30%. The serum bilirubin level reached a maximum of 19.9 mg.%, with 8.2% direct fraction. The cholesterol (total) level rose to 410 mg.%; the alkaline phosphatase level was 19.4 Bodansky units. The SGO-T value decreased to 50 units, and both cephalin flocculation and thymol turbidity remained normal.

By the second week all evidence of ecchymosis had disappeared. The patient was permitted out of bed on the 21st day, and by the 28th day clinical evidence of jaundice had disappeared. Proctoscopy just prior to discharge revealed complete healing of the eroded hemorrhoid. On the 42nd day after admission the patient was discharged to the clinic, where she was followed for three months with no recurrence of jaundice or evidence of further bleeding.

Comment

There can be little doubt concerning the basic diagnosis of chlorpromazine-induced jaundice. The clinical appearance of jaundice on or about the 17th day of drug ingestion is typical. The chemical laboratory data are equally typical, showing hypercholesteremia and hyperphosphatemia (alkaline) with normal flocculation tests and relatively little rise in the SGO-T level. The degree of hyperbilirubinemia (up to 19.9 mg.%) is well within the zone attained when jaundice is associated with this drug.

The hyperglycemia appeared to be an independent finding related to a coincidental occurrence of diabetes mellitus. The peripheral blood findings (normal white blood cell count with minimal polynucleosis) is quite compatible with this diagnosis. The frequent finding of eosinophilia was not fulfilled in this instance. Biopsy of the liver, not attempted until the 37th day in the hospital, unfortunately was of no practical assistance because of the insufficient tissue obtained. It is entirely possible, of course, that by this time the histological picture might no longer have been diagnostic or even abnormal.

A striking observation by the medical attendants in this case was the appetite manifested by this patient almost from the first days in the hospital, when the bleeding had quieted down and feeding by mouth was resumed. It was a situation which evoked considerable comment by physicians and nurses: she fairly leaped at her tray and devoured all food in sight rapidly, uninterruptedly, and completely. This could hardly be explained by her history of thyroid disease, and she was found to be euthyroid in the current period of hospitalization. We had not observed this in previous cases of chlorpromazine-induced jaundice, nor does the literature remark on it.

Nothing resembling this excessive hunger and appetite is ordinarily observed in hepatitis of viral origin. Occasionally in the recovery stage of acute viral hepatitis, excessive food intake becomes a problem in the future management of the patient because of the tendency to rapid and extreme weight gain[10] but is ordinarily not seen from the peak of the illness. However, in our experience with chlorpromazine-induced jaundice, it is highly characteristic to observe relative well-being almost from the onset of the illness. Disproportion exists between the depth of the jaundice and the relative lack of discomfort and complaint by the patient, with the possible exception of pruritus early in the illness.

Hemorrhage is an exceedingly rare manifestation of chlorpromazine-induced hepatitis with jaundice, as has already been pointed out, and is only slightly less infrequent in the patient receiving this drug who does not develop jaundice. In our jaundiced patient the bleeding appeared from four sites, being of major importance from the rectal mucosa and less prominent in the vagina, the urinary tract, and skin over the knees. The cause is not absolutely clear, but in the absence of a more satisfactory alternative explanation a likely one is hypoprothrombinemia. Absolute proof of the existence or lack of existence of such hypoprothrombinemia at the onset of hemorrhage is lacking because of the unfortunate technical deficiency in handling the blood sample drawn soon after the occurrence of the rectal hemorrhage and prior to the administration of the vitamin K_1. About seven hours had elapsed by the time another sample of plasma had been obtained for prothrombin time determination. The reading was then 14.1 seconds with a control of 12.8 seconds. Twenty-four hours later it was 13 seconds, equal to the control.

When vitamin K_1 is administered intravenously, bleeding is usually controlled within 3 to 6 hours, and a normal prothrombin time (if previously markedly elevated, enough to initiate hemorrhage) may often be obtained within 12 to 14 hours. It cannot be concluded beyond question that the assumed plasma prothrombin diminution was thus restored toward normal by the vitamin K_1. Nonetheless, it is tempting to make this assumption because of the later (secondary?) rise in prothrombin time to 16 seconds, when next tested a week later on the 11th hospital day. However, it is recognized that seven hours is ordinarily too brief a period in which to anticipate a considerable reduction in the prothrombin time by means of vitamin K therapy, although it may occur.

The mechanism whereby such reduction of prothrombin time might have been accomplished by parenterally given vitamin K_1 is not fully clear. Generally it is felt that the hepatic involvement due to chlorpromazine is a result of a sensitivity reaction with consequent interference with the normal flow of bile from liver cell to bile radicle. In viral hepatitis, toxic hepatitis, and other diseases in which the parenchyma of the liver is diffusely injured or destroyed, the reduced plasma prothrombin content responds little or not at all to vitamin K. On the other hand, in case of biliary obstruction or of bishydroxycoumarin-induced reduction of plasma prothrombin content, the effect of parenterally given vitamin K is to correct the prothrombin deficiency.

Thus, if a reduced prothrombin content in the blood was counteracted or corrected by vitamin K_1 in our case, it is fair to conclude that the inflammatory reaction in the liver due to chlorpromazine must differ from that occurring in viral hepatitis. This conclusion is supported by our knowledge of the difference in the histology of the liver in these two disease states.

It should be stressed that in diseases of the liver there are factors in blood coagulation other than prothrombin, such as proconvertin (factor VII) and accelerator globulin (factor V or proaccelerin). Our measurement of prothrombin time by the Quick method does not delineate the respective roles and presence of these additional factors.[11] All these factors affect the prothrombin time, and when we demonstrate a deficiency in prothrombin we cannot be certain which is at play.

In the face of the jaundice, in the absence of recognition of any other factor promoting bleeding, such as platelet deficiency, and in view of the rapid cessation of bleeding on administration of vitamin K_1, we are inclined to believe that hypoprothrombinemia was the cause. It has already been pointed out that this is an extremely rare finding in the experience of those who have measured prothrombin activity in chlorpromazine-induced hepatitis. The few instances of bleeding associated with the use of chlorpromazine have been mild and observed almost exclusively without the development of jaundice. The rarity of this occurrence is the reason for recording this experience.

Summary

A 66-year-old diabetic woman bled from multiple sites (rectum, vagina, urinary tract, and skin) in association with jaundice induced by chlorpromazine, administered for 17 days. The likely explanation for the hemorrhage is hypoprothrombinemia, although there is a possibility of defects in other coagulation factors. Note is taken that depressed prothrombin activity after chlorpromazine ingestion is uncommon. Hemorrhagic manifestations in association with the administration of chlorpromazine are rare. Particularly is this infrequent in reported cases of jaundice. Minor bleeding has been noted in the absence of jaundice, usually in the form of purpura. A striking clinical observation in this patient was the voracious appetite she manifested from the height of her illness.

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OTOTOXICITY OF KANAMYCIN

REPORT OF THREE CASES

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Severe and apparently permanent loss of hearing was observed in three patients who received kanamycin in the treatment of serious infections. One man, aged 46 years, received 40 Gm. in the course of 16 days; another, aged 62, received 14 Gm. in the course of 7 days. In these cases tinnitus preceded the impairment of hearing. A woman aged 55 received 14 Gm. in two courses separated by an interval of five days. In her case there was no warning tinnitus. In all cases the deafness progressed after administration of the kanamycin was stopped; loss of hearing has been practically complete, and no improvement has been found at later examinations.

The new antibiotic kanamycin, discovered by Umezawa in 1957, is still under clinical observation, and we believe that all serious toxic effects should be reported in order to establish its uses and limitations. This is necessary in the study of any new antibiotic, inasmuch as these are frequently coming on the market.

Report of Cases

Case 1.—A 46-year-old man was admitted to the hospital because of hematemesis of 24 hours' duration. About 15 years previously the patient had had paratyphoid. Two years ago he was operated on because of a hernia of the nucleus pulposus, with good results.

Present Illness.—The patient stated that about five years previously he began to notice epigastric discomfort two to three hours after meals; this was relieved by taking food or antacids. The pain became worse and was so severe that the patient was awakened at night. His physician treated him for peptic ulcer, in spite of negative findings of roentgenographic study. He improved with this medication, although he said that he had periods of pain in the same area which were rapidly relieved by taking antacids. After the treatment he had another series of roentgenographic studies of the stomach and again the findings were normal.

Two years before the present admission, when he had been in Johns Hopkins Hospital for an operation on the spinal column, the patient had another roentgenographic study and for the first time was told that he had a healed duodenal ulcer. The roentgenogram showed a deformity of the duodenum.

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He felt all right until three months before admission, when he again had epigastric pain, relieved by taking food or antacids. Twenty-four hours before admission the patient felt weak and noticed black stools for the first time. Four hours before admission he felt extremely weak and dizzy, vomited blood, and became very pale. A physician was called and found him in mild shock; he was therefore referred to the British American Hospital for further treatment.

Physical Examination.—On admission the patient was pale, perspiring profusely, and somewhat nervous. His blood pressure was 80/40 mm. Hg, pulse 120, and respirations 24 per minute. The physical examination was noncontributory except for signs of mild shock. He immediately received a blood transfusion. In two and one-half days he received a total of 2,000 cc. of blood, after which the hematocrit fluctuated between 25 and 26%, and the hemoglobin concentration between 8.26 and 8.58 Gm.%. More transfusions were given until the hemoglobin value became 11.74 Gm.% and the hematocrit 38%, so that he could be operated on on his third hospital day.

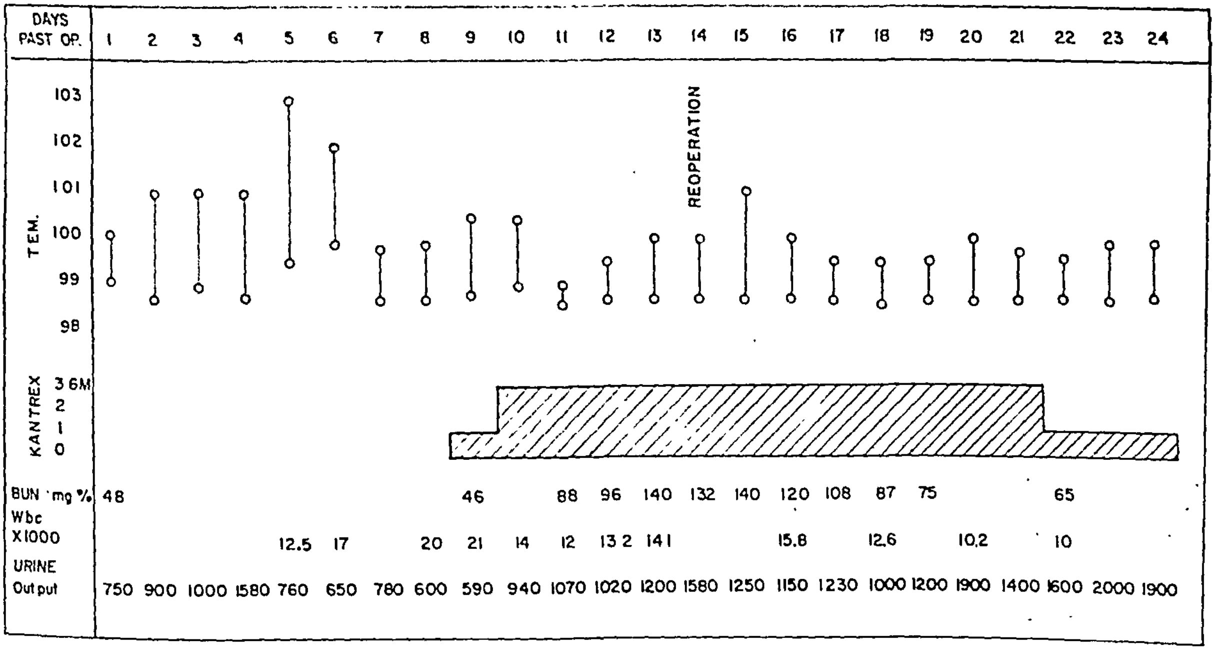

Fig. 1 (case 1).—Chart showing temperature, urinary output, blood urea nitrogen level, and white blood cell count in relation to administration of kanamycin (Kantrex).

An extensive gastrectomy (Hofmeister-Finsterer) was performed. By the time the patient returned to his room the hemoglobin level was 11 Gm.% with a hematocrit of 39%. The patient then received 1 Gm. of oxytetracycline intravenously for three successive days, during which period his temperature fluctuated between 99 and 100 F (37.2 and 37.8 C). It became normal on his fourth postoperative day, and the antibiotic therapy was discontinued. He was doing well except for the pulse, which remained between 100 and 110 per minute. The laboratory studies before the operation showed normal coagulation, bleeding, and prothrombin times. Blood urea level was 48 mg.%, the urine was normal, and the serologic examinations gave negative results. His blood was type O, Rh-positive.

Twenty-four hours after the antibiotic therapy was discontinued, on the fifth postoperative day, the patient had a chill and his temperature rose to 103 F (39.4 C); the pulse was then 140 and respirations 30 per minute, and blood pressure was 120/80 mm. Hg (fig. 1). The white blood cell count was 17,000 per cubic millimeter, with 86% neutrophils. Results of two blood cultures taken on that day and the following day were negative. Urine examination also gave a negative result. Blood urea nitrogen level was 46 mg.%. The patient was then given crystalline penicillin, 500,000 units every six hours. His temperature improved with this therapy, but the patient's condition remained toxic; the pulse was 110 and 120 per minute. It was then evident he was suffering from a severe infection. The white blood cell count had increased to 20,000 per cubic millimeter, with 83% neutrophils. On the ninth postoperative day, because the patient continued with severe tachycardia, tachypnea, fever, and vomiting for 48 hours, it was decided to use kanamycin (Kantrex). The first day he was given 1 Gm. but from then on a total of 3 Gm. per day was given for 12 days. When he complained of tinnitus the kanamycin dosage was reduced to 1 Gm. a day for the next three days. He received a total of 40 Gm. over the period of 16 days.

During the administration of the antibiotic daily urine examinations were carried out, but no major damage to the kidney could be detected. The hematological values became normal and the elevated blood urea nitrogen level, which was interpreted as indicating prerenal azotemia, dropped gradually. On his 10th postoperative day, 24 hours after kanamycin therapy had been started, the surgical wound began to drain profusely, and a culture of the exudate was positive for coagulase-positive Staphylococcus pyogenes var. aureus. This staphylococcus was sensitive to chloramphenicol, erythromycin, and kanamycin and resistant to eight other antibiotics.

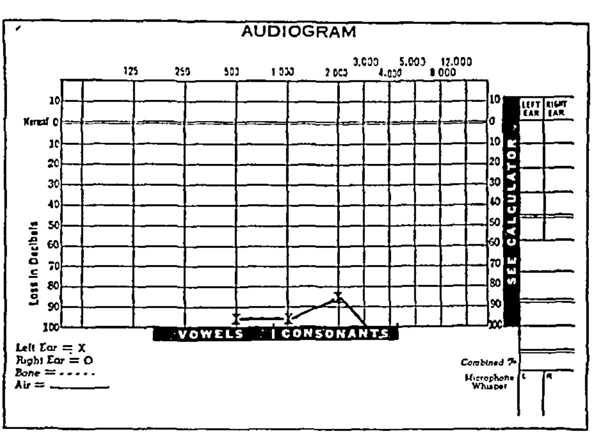

Fig. 2 (case 1).—Audiogram taken on 17th postoperative day.

On the 12th day of administration, the 22nd hospital day, after he had received 37 Gm. of kanamycin, he started having ringing of a high pitch in both ears. Twenty-four hours later he noted loss of hearing that rapidly increased so that in 48 hours he "heard nothing." The nasal mucosa was reddened, there was pus present in the tonsils, and bilateral cerumen was washed out. Both eardrums were retracted and a whitish deposit was noted at the posterior superior quadrant of the left eardrum. An audiogram made at this time (fig. 2) showed severe bilateral deafness. There was no discrimination whatsoever in hearing for speech even at 100 db. in either ear. On his 14th postoperative day the patient was taken to the operating room, the wound was reopened, and a large subhepatic abscess was found and drained. After this the patient's pulse and temperature gradually came down and his condition improved until his discharge after 30 days in the hospital.

There was no history of the patient's ever having received streptomycin or neomycin. The pathologist's report on a specimen from the stomach was hemorrhagic gastritis; no ulcer was found. The patient's progress has been followed for two months and he has been symptom-free from the gastrointestinal point of view, but the damage to the eighth nerve has continued, with total deafness (fig. 3).

Case 2.—A 62-year-old man came into the hospital because of urinary infection and renal failure. He had had repeated attacks of urinary infection since childhood, with several attacks of renal lithiasis. He had undergone a nephrectomy because of renal stones 12 years previously. He had been known to be hypertensive for the past three years.

Present Illness.—About four weeks before admission he developed a severe epistaxis, requiring posterior packing of the nose and surgical cauterization of the mucosa. His blood pressure was 200/130 mm. Hg, and the blood urea nitrogen level was 170 mg.%. Because urine culture gave a positive result he was given nitrofurantoin (Furadantin), with poor results, and then 1 Gm. of kanamycin twice a day. He received a total of 14 Gm. When the patient had received 12 Gm. he began to notice tinnitus, and although the drug therapy was discontinued he developed almost complete deafness in four days. Hearing was normal prior to treatment. Pus was found on pressure of the tonsils, and both eardrums were thickened and whitish. Crusts were present in the right nostril. An audiogram showed a severe hearing loss for the right ear (fig. 4), but an island of decibels for 1,000 cycles in the left. The patient received, besides kanamycin, vitamin K and a lipid-protein thromboplastic agent (Clauden) as the only other medicaments. He denied any previous ear trouble or ever having received streptomycin or neomycin.

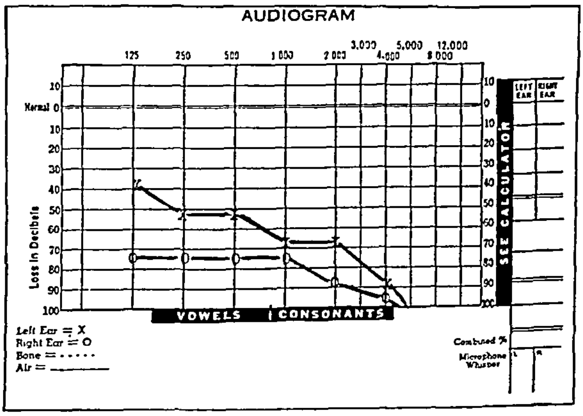

Fig. 3 (case 1).—Audiogram taken eight days after therapy with kanamycin was discontinued.

Physical Examination.—The patient looked ill, and his mucous membranes were pale and dry. Lungs were normal to percussion and auscultation. The heart was normal and blood pressure was 200/110 mm. Hg. The laboratory tests made on admission showed hemoglobin level to be 7.62 Gm.%; red blood cell count, 2,610,000 per cubic millimeter; white blood cell count, 6,950 per cubic millimeter, with eosinophils 6%, neutrophils 74%, lymphocytes 13%, and monocytes 7%. The red blood cell count showed some *polychromatophilia and* anisocytosis. Coagulation time was 8½ minutes, bleeding time 1 minute. His blood was type O, Rh-positive. The blood urea nitrogen level on admission was 86 mg.% and blood creatinine level, 5.1 mg.%. Serologic examination gave a negative result. Urine showed a specific gravity of only 1.005; there was 2+ albumin and the sediment showed white and red blood cells with occasional granular casts. The urine culture was positive for Staph. aureus, coagulase-positive and sensitive to chloramphenicol, novobiocin, and tetracycline but resistant to other antibiotics. The electrocardiogram showed slight abnormality which was interpreted as consistent with an elevated serum potassium level.

Course in Hospital.—The patient remained in this hospital for one week. He showed a daily low-grade fever and his blood pressure fluctuated between 160/100 and 200/110 mm. Hg. He received a transfusion of 500 cc. of blood and a 250-mg. dose of chloramphenicol every six hours. He was discharged slightly improved. When seen four months later he had severe signs of uremia and the deafness had continued with the same intensity.

CASE 3.—A 55-year-old woman stated that three months before admission she had begun to vomit and had epigastric distress without relation to food or time of day. When the attacks of vomiting recurred a physician found that she had hypertension. During the past six years she had had some dyspnea on exertion, and she had noted loss of weight in the past six months. We were unable to obtain a history of her having received streptomycin or neomycin.

Physical Examination.—On admission to hospital the patient was obese; her skin was dry and there was edema of the eyelids as well as the ankles. The blood pressure was 170/100 mm. Hg. The blood sugar level, which had been 230 mg.% two months before admission, was 105 mg.%. Blood urea nitrogen level was 68 mg.%. The urine showed a few leukocytes, red blood cells, and granular and hyaline casts. A urine culture was reported positive for Escherichia coli, sensitive to nitrofurantoin, kanamycin, chloramphenicol, and tetracycline.

Course in Hospital.—On her sixth hospital day, because of positive urine culture, she received 2 Gm. of kanamycin, then 1 Gm. each day for the next six days. The urine culture remained positive and on her 18th hospital day kanamycin therapy was resumed, 2 Gm. the first day and 1 Gm. on the three successive days. After receiving a total of 14 Gm. she complained of deafness, and, although the drug therapy was discontinued immediately, she rapidly developed total deafness. The audiogram was reported negative for both ears in air as well as bone conduction.

Comment

It is known that neomycin is nephrotoxic and neurotoxic[1] and that kanamycin has a similar chemical structure and similar antibiotic behavior, since there is complete cross-resistance between the two antibiotics[2]; therefore it seemed quite possible that kanamycin would be toxic for the kidney as well as for the ear. It is interesting that kanamycin has an incomplete cross-resistance with another neurotoxic antibiotic, streptomycin. The literature indicates that kanamycin has a definite toxicity for animals[3] as well as for man, producing damage to the kidney,[4] affecting the tubular and glomerular function,[5] and damaging the eighth cranial nerve.[6] At present the exact toxic dosage of kanamycin has not been established, but it seems to depend not only on the total amount administered but also on the dose given per day.

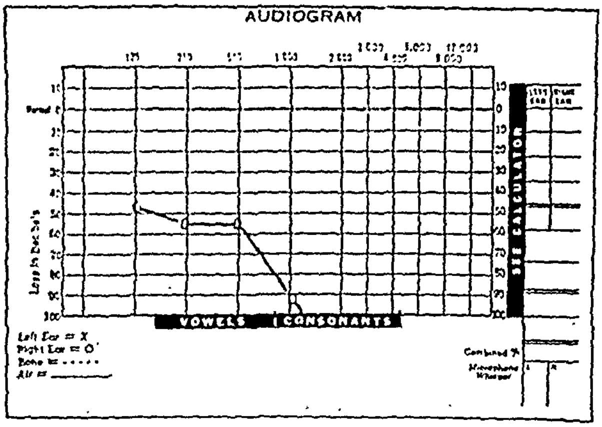

Fig. 4 (case 2).—Audiogram taken two weeks after therapy with kanamycin was discontinued.

Bunn and Baltch,[7] reporting on 15 patients, observed no side-effects from kanamycin when 1 Gm. was given daily for 3 to 17 days. The same authors observed the toxicity to be of a minimal order when the drug was given for less than three weeks in doses that varied between 0.5 and 3.0 Gm. per day. Above this level they observed eosinophilia, urinary abnormalities, and damage to the eighth nerve, particularly when the total amount of kanamycin received by the patient was between 40 and 50 Gm.[4a] Other investigators[8] report no toxic effects with daily doses of 1 to 2 Gm., but if the time of administration is prolonged to six months, even though the daily dose is reduced to 0.5 Gm., damage to the auditory nerve is produced.[4b] Donomea[6a] found audiometric impairment in 20% of the patients who received over 6 Gm. of kanamycin per week, but he was able to reduce this toxicity to 4% if the amount of the antibiotic was less than 6 Gm. per week.

In our report, in case 1, kanamycin was administered in the maximum recommended dose. The patient had a prerenal azotemia, as proved by the return of the blood urea nitrogen level to normal values. As soon as the intra-abdominal abscess was drained, and while the administration of kanamycin continued, there was no decrease in the urinary output and the blood creatinine level remained normal. The total amount of kanamycin that the patient received was 40 Gm. in 16 days, and the symptoms of injury to the eighth nerve appeared when he received 37 Gm.; therefore, the ototoxicity became evident before the level that has been pointed out as toxic was reached.[7]

In the other two cases presented here serious renal lesions existed before the administration of kanamycin. In case 2 the total amount of kanamycin given to the patient was 14 Gm. in seven days, with impairment of hearing becoming evident after he had received 12 Gm. In case 3 the damage seemed more marked, since the total amount of the antibiotic was only 14 Gm., administered in two periods, with an interval of five days of no kanamycin administration. The signs of deafness became noticeable during the second course of treatment with only 4 Gm. of kanamycin. This last case is suggestive of a hypersensitivity to the antibiotic or a cumulative toxic effect due to the patient's renal failure.

Common to our three cases was the progressive damage to the auditory nerve, which appeared to be irreversible and which continued even though kanamycin therapy was discontinued at the first signs of damage.

The number of cases presented here is too small to permit conclusions to be drawn, but the accumulation of this type of information should establish the position of this new antibiotic in clinical practice and clearly determine its limitations.

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HAZARDS OF MERCY.—From time to time reports appear in the newspapers of what are described as "Mercy Flights." They are usually undertaken to convey someone from an outlying area to a larger centre where he can obtain urgently needed special medical attention or to rescue someone in danger of his life, for example, from flood. A number of such flights have ended in disaster, perhaps with loss of the lives of all concerned, and no doubt many people have wondered what lay behind these tragedies. . . . Since the majority of Mercy Flights intimately concern members of the medical profession, it is vital that they should understand what such flights involve and the conditions under which they may be undertaken. . . . While medical emergencies can arise at any time, the aircraft mostly used in this work can be flown with normal safety only in daylight and fair weather. Most medical or ambulance flights take place under visual flight conditions and are perfectly normal operations with an excellent safety record. It is the minority which become Mercy Flights that constitute the problem. The difficulties outlined here could be reduced by an understanding on the part of the doctor of the pilot's problems, and by a readiness to discuss with the pilot the medical aspects of a flight proposed at night or in bad weather—that is, by definition, a Mercy Flight. —Mercy Flights and Their Safety, editorial, *The Medical Journal of Australia,* Jan. 24, 1959.

CONSCIOUSNESS AND PAIN DURING APPARENT SURGICAL ANESTHESIA

REPORT OF A CASE

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A patient underwent an operation under general anesthesia which included the use of succinylcholine and intravenously given lidocaine, with assisted respiration. After recovery she gave evidence of having been intermittently conscious during the three-hour period of supposed anesthesia and stated that she had suffered extreme pain during much of the operation. An awareness that such an extreme in pain reflex threshold may rarely exist in patients undergoing operative procedures should caution us to be more appreciative of the subtle signs suggesting an inadequate state of anesthesia. This is particularly applicable when respiratory reflexes and other types of response are obviated by the use of neuromuscular blocking agents.

The introduction of curare as a neuromuscular blocking agent in clinical anesthesia by Griffith and Johnson[1] in 1942 set the stage for radically different concepts in the practice of surgical anesthesia. Here was a means whereby satisfactory anesthesia could be offered to the most demanding of surgeons without the necessity of maintaining high blood and brain tissue levels of inhalation or intravenous anesthetic agents. The demonstration by Foldes and co-workers[2] of the close control of neuromuscular paralysis afforded by a continuous infusion of dilute succinylcholine gave more widespread popularity to and promoted acceptance of this school of practice. In 1955 Artusio[3] introduced the technique of ether analgesia and described the homeostatic benefits derived by maintaining a level of anesthesia at which the patient was capable of responding to questions and of discriminating subjective senses of taste and color.

The combination of minimal central nervous system narcosis plus neuromuscular blockade has received increasing acceptance by clinical anesthesiologists throughout the United States and abroad during the past 10 years. We have utilized this form of anesthesia in several thousand surgical and gynecologic operations and have been favorably impressed with it as a technique providing a smooth course of surgical anesthesia, with a minimum of side-effects and a short postoperative waking time. After such an anesthetic procedure there occurred recently on our service a complication which brought forcibly to our attention a potential hazard involved in this concept of anesthesia, which we feel is of sufficient importance to be reported.

Report of a Case

The patient was a 40-year-old woman who entered the hospital with the diagnoses of cystocele and rectocele. She was scheduled for a vaginal hysterectomy and an anterior and posterior colporrhaphy. Her operative history included a tonsillectomy as a child and an appendectomy at the age of 16 years, both under gas-oxygen-ether anesthesia. She had had four vaginal deliveries. For the first three of these she had had gas-oxygen-ether anesthesia, and for her fourth and last delivery a saddle-block technique had been used. During one of the pregnancies she had been given paraldehyde in an early and quiescent phase of labor, had become agitated, and had had intense and vivid recollections of her pain after this medication. Administration of codeine and meperidine at various other times resulted in extreme episodes of nausea and vomiting. Administration of erythromycin, two years prior to admission, had caused a skin eruption. Three years prior to admission she was hospitalized with a tentative diagnosis of pericarditis, but studies did not confirm this impression and it was decided that the presenting symptoms were emotionally based.

Physical findings on the present admission were normal except for the pelvic and perineal disease for which the operation was to be performed. Her hemoglobin concentration was 11.7 Gm. % (81%), and white blood cell count 6,800 per cubic millimeter with 48% polymorphonuclear cells, 50% monocytes, and 1% basophils. The hematocrit was 38%. Blood glucose level was 86 mg.%, blood urea level 35 mg.%. Urinalysis revealed nothing abnormal; specific gravity was 1.013.

The patient was given, as bedtime sedation the evening before the operation, secobarbital and amobarbital (Tuinal), 100 mg., and perphenazine (Trilafon), 4 mg., each by mouth. In view of her his-

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tory of side-reactions to opiates no narcotic was given preoperatively, the medication consisting of 5 mg. of perphenazine and 0.4 mg. of atropine intramuscularly one hour before the induction of anesthesia. Bearing in mind also the history of recent emotional problems it was decided that a general anesthetic would be indicated for the anticipated operative procedure.

Anesthesia was induced with intravenous administration of thiopental, 200 mg. in a 2% solution. The patient was given a continuous intravenous infusion containing 0.1% lidocaine and 0.025% succinylcholine. Nitrous oxide and oxygen at a 4-liter and 2-liter flow, respectively, in a semiclosed circle-absorber system was then administered under a mask. Respirations were spontaneous but assisted throughout the course of anesthesia. The operative procedure lasted two hours and 50 minutes and the anesthesia three hours and 10 minutes. During this time a total of 400 mg. of thiopental, 500 mg. of succinylcholine, and 2 Gm. of lidocaine were used. A no. 3 oropharyngeal airway was inserted early during the procedure and removed at the end before the patient left the operating room. The systolic blood pressure was 120 mm. Hg before the induction of anesthesia and ranged between 115 and 130 mm. Hg during the entire procedure. The pulse rate ranged from 84 to 100 per minute. The blood loss was appreciably more than usual, and this was commented on by the members of the operating team.

Two 500-cc. units of blood were administered during the operation. The color of the patient and of the blood was good at all times and the anesthesia progressed uneventfully. It was noted that there were occasional episodes of resistance to inspiratory assistance. At one point during the operation the patient (in a lithotomy position) suddenly moved her right leg.

The patient was responding and talking to visitors within 10 minutes of leaving the operating room. Her blood pressure remained a little low during much of the afternoon (88 to 100 mm. Hg systolic), but the pulse was slow and her skin was warm and dry, although she appeared slightly pale. There was little nausea, and no vomiting was noted by the nurse or remembered by the patient during the postoperative period. She received during the first three days a total of 25 mg. of morphine and 10 mg. of perphenazine, in divided doses.

Despite this apparently uneventful anesthetic course the patient had a most unpleasant experience to relate to the surgeon and the anesthesiologist. She had been intermittently conscious and unconscious during the three-hour anesthetic period. She volunteered the information that an airway had been inserted in her mouth and removed at some later time. She reconstructed details pertaining to the discussion of the blood loss and the decision to start administration of the second unit of blood. She also experienced dull, unbearable pelvic, lower back, and perineal pain during much of the operation.

Comment

There is little doubt in the minds of the attending physicians that the patient was conscious during phases of this procedure and suffered considerable discomfort. As this was the first such case in our experience, we have reviewed critically the management of the entire anesthetic procedure including the preanesthetic medication, the agents and proportions used, the mechanical accuracy of the anesthesia apparatus, the background of the patient, and our own ability to evaluate the adequacy of anesthesia under the situation described.

Galla and co-workers[4] have recently reevaluated the traditional signs of anesthesia as they might apply to newer anesthetic agents and techniques. Nearly all of our signs of anesthetic depth are dependent on the muscular response to some type of stimulus, whether exogenous, provoked by the observer, or endogenous, as a result of physiochemical changes at the vital centers. While the patient is under neuromuscular blockade such signs are either eliminated or dampened to the point where they become less easily recognized. Galla and co-workers stressed the importance of two signs indicating light planes of anesthesia in the patient under curare anesthesia. The first of these is increased resistance to inflation of the lungs, which is associated with Courtin and co-workers' electroencephalographic level 1[5]; the second is pupillary dilatation in response to surgical stimulus. This same author pointed out that alternative etiological factors leading to pupillary dilatation are excessively deep planes of anesthesia and anoxia.

Artusio[3] has demonstrated that in plane 2, stage 1 of ether analgesia, although a patient is still responding to questioning and reacting to surgical stimulus with gross movements, there is complete amnesia on postoperative questioning. Facial grimacing and movements of an extremity are signs frequently seen during analgesic techniques, whether the primary anesthetic agent is nitrous oxide or ether.

In the case described in this report pharyngeal and corneal reflexes were absent, and respirations were depressed to the point of requiring some assistance. These several signs suggested a surgical depth of anesthesia. There was maximal pupillary constriction throughout the course of the anesthesia, which has been a consistent finding in our patients who receive intravenous thiopental, succinylcholine, and lidocaine combined with a nitrous oxide and oxygen inhalation anesthetic, and which would not have suggested an unduly light plane of anesthesia. Any degree of pupillary dilatation would have caused us to be concerned about the adequacy of our ventilating technique or about the possibility of an adverse response of the patient's cardiovascular and cerebrovascular mechanisms to a surgical or an anesthetic insult.

Although the patient was breathing spontaneously throughout the anesthetic course, there were periods of increased resistance to lung inflation while inspiration was assisted and occasional episodes of sudden change in rate and depth of breathing. These phases of her respiratory pattern were the only indications of light anesthesia. In addition, as was noted in the protocol, the patient made a sudden movement of her right leg at the time the surgeon made his initial incision in the posterior vaginal mucosa to repair the rectocele. This occurred 30 minutes before the end of the entire operative procedure. Such a plane of anesthesia was not considered undesirable; it caused no impediment to the surgical procedure and allowed for full compensatory response to the not inconsiderable blood loss being suffered by the patient. With the basal narcosis of intravenously given thiopental and an apparent metering of two-thirds nitrous oxide in a total flow of 6 liters, it was felt that there was no chance that the patient would not receive complete analgesia and amnesia for the operative procedure.

A review of the present case serves to caution us that, in our efforts to make possible surgical intervention with a minimum of homeostatic disturbance, the anesthetic or pain-reflex threshold of the patient may be at such a level that we are actually administering inadequate amounts of depressive agents to obtain the desired degree of analgesia and amnesia. It should be emphasized that signs of unduly light anesthesia may be most subtle and that the analgesic techniques utilized may be accompanied by the inherent risk of a conscious and uncomfortable patient. The use of the neuromuscular blocking agents amplifies the chances of this situation occurring. Perhaps the addition of an opiate to the preanesthetic medication may have sufficed to have given the patient the required amount of basal narcosis. The importance of the preoperative opiate in a nitrous oxide anesthesia has been stressed by Clement,[6] although in recent years much has been written concerning the iniquities of prescribing opiates to the patient going to surgery.[7] A larger dose of thiopental than the 400 mg. used for the three-hour procedure would certainly have been justified and could have induced the additional anesthetic depth necessary. However the deeper anesthesia is accomplished, greater concern when confronted with the signs of light anesthetic planes may help to avert subsequent experiences such as the one just described.

Summary

A patient under apparent anesthesia for a prolonged perineal operation suffered indisputable phases of consciousness and extreme pain. Pertinent aspects of the analgesic techniques in anesthetic management include a consideration of the interpretation of the signs of anesthesia as they might apply to our new anesthetic agents and methods, especially the role of the neuromuscular blocking agents in affecting the signs of anesthetic depth. Although the minimal effect on homeostasis of the newer anesthetic techniques is of recognized value, an awareness of the possibility of an anesthetic experience such as the one described should serve to make us pay greater heed to signs of light planes of anesthesia.

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NAUSEA AND VOMITING IN THE IMMEDIATE POSTANESTHETIC PERIOD

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Factors that might determine the incidence of nausea and vomiting were sought in a study of 1,602 patients recovering from general anesthesia. Vomiting was somewhat less frequent in older patients than in younger ones and much less frequent in men than in women. Comparisons between anesthetics were difficult because the type of operation influenced the choice of anesthetics, but under the conditions of this study the use of ether was followed by a slightly lower incidence of vomiting (23.3%) than was the use of cyclopropane (24.1%). Endotracheal intubation and administration of relaxants had no appreciable effect, but insertion of a gastric tube reduced the incidence of vomiting from 25.3 to 15%.

Every general anesthesia is composed of three parts: induction, maintenance, and emergence or recovery. Many clinical and laboratory studies on the first two phases of anesthesia have been reported, resulting in improvements in anesthetic techniques. Patients can now be anesthetized for surgery considered impossible only a few years ago. These improved results are related to new agents, improved techniques and apparatus, and increased knowledge in the fields of physiology, pharmacology, and chemistry related to anesthesia. In contrast to this, relatively little work has been done in relation to the period of emergence from anesthesia.

The introduction of the postanesthesia recovery room has been a significant advance in postoperative care of the surgical patient. Patient safety has been increased by the presence of specially trained nursing personnel familiar with patient care during this critical period. In 1899 Blumfeld wrote, "A patient's dread of operation is often due more to his fear of anesthesia than to the operation itself."[1] The fear of anesthesia is mostly caused by the anticipation of the unpleasantness of the postanesthesia recovery phase. It matters little to the average patient that he received a skillful anesthesia, requiring possibly several hours of constant vigilance and care in order to provide and maintain normal physiology throughout an operative procedure. Rather, the patient's concern is associated with what he experienced when he regained consciousness, and frequently the difficulties of this period are ascribed to anesthesia.

Dripps[2] observed in 1949 that there was "little significant information on such a commonplace problem as the incidence of nausea and vomiting following the administration of an anesthetic." Because of the many variables involved, such as premedication, anesthetic agent and method of administration, duration of anesthesia, type of operation, and age, sex, physical status, mental status, constitution, and habitus of the patient, the task of studying the postanesthesia recovery is a difficult one. This investigation was undertaken in order to collect more information on this important period.

The study was divided into three major parts: observations related to nausea and vomiting, observations related to the mode of recovery, and observations related to blood pressure. This particular report deals only with the observations concerning nausea or vomiting. All data obtained were analyzed and correlations were made between some of the many variables related to anesthesia and surgery; specifically, the possible relationship between physical characteristics of the patient, age, sex, and body structure, and type and duration of operation.

Procedure

Special study sheets, composed of two parts, were filled out in conjunction with the anesthesia record of each patient. The first section was completed by the person administering the anesthesia. For classification of the structural type the following criteria of body structure based on Kretschmer's[3] work were used: narrow, slender (leptosome); rounded, chubby (pyknic); muscular, well-developed (athletic); and with grossly abnormal proportions or deviations (dysplasic). These records then accompanied the patient to the recovery room, where they were completed by the recovery room personnel under the supervision of an anesthesiologist. The recovery room nursing staff had no precise knowledge of the objectives of this study, so their observations may be presumed to be unbiased.

Notations concerning nausea and vomiting were based only on objective signs. Vomiting was recorded whenever the expulsive efforts produced even a small amount of material. Nausea was re-

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corded when a patient was complaining of a desire to vomit or when expulsive but unproductive vomiting movements were observed. Nausea is a subjective experience which may or may not be associated with vomiting or retching; retching is defined as spasmodic contractions of the respiratory and abdominal musculature without expulsion of any material. We use the term nausea in this paper to designate the two phenomena. The patients were asked no questions related to nausea and vomiting, in order to avoid any suggestion in the matter. The patients were discharged from our recovery room when they were alert, with stable vital signs, and oriented as to time and place. The average time for this ranged from two to three hours.

The completed data sheets were coded and the results reported on IBM cards; these cards were used later for tabulation, correlation, and analysis. Complete observations and data were obtained on 1,602 patients of all ages. Of these 752 were males and 850 were females. Five age groups were used in the study: group 1, aged 10 and under, comprising 152 patients, 101 boys and 51 girls; group 2, aged 10 to 17, comprising 64 patients, 44 boys and 20 girls; group 3, aged 18 to 49, comprising 623 patients, 194 men and 430 women; group 4, aged 50 to 65, consisting of 483 patients, 250 men and 232 women; and group 5, aged over 65, consisting of 280 patients, 163 men and 117 women.

Table 1.—*Distribution of Anesthetic Agents by Age and Sex of Patient*

Age Groups, Yr.	Thiopental-Nitrous Oxide			Ether			Cyclopropane			Cyclopropane-Ether		
	Total	M	F	Total	M	F	Total	M	F	Total	M	F
11-17	9	6	3	15	11	4	24	16	8	15	11	4
18-49	86	38	48	88	41	47	329	70	259	120	44	76
50-65	99	65	34	108	51	57	162	84	78	108	49	59
over 65	78	57	21	85	47	38	65	29	36	51	30	21
Total	272	166	106	296	150	146	580	199	381	294	134	160

Ninety-seven per cent of the patients were given premedication with barbiturate and belladonna preparations, usually amobarbital (Amytal) sodium and atropine. Only 3% received an opiate in lieu of or in conjunction with the barbiturate or belladonna. Four anesthetic agents were used: a combination of thiopental and nitrous oxide; ether; cyclopropane; and cyclopropane with ether. Their distribution is reported in table 1.

Duration of Anesthesia.—In 408 patients (153 males and 255 females) the duration of anesthesia was one hour or less; in 479 patients (249 males and 230 females) it was one to two hours; in 287 patients (123 males and 164 females) two to three hours; in 172 patients (74 males and 98 females) three to four hours; and in 104 patients (52 males and 52 females) the procedure took over four hours. Results were analyzed by means of the chi-square test; the following criteria were used for p values: $p<0.01$ considered significant, $0.01<p<0.02$ considered of borderline significance, and $p>0.02$ considered insignificant.

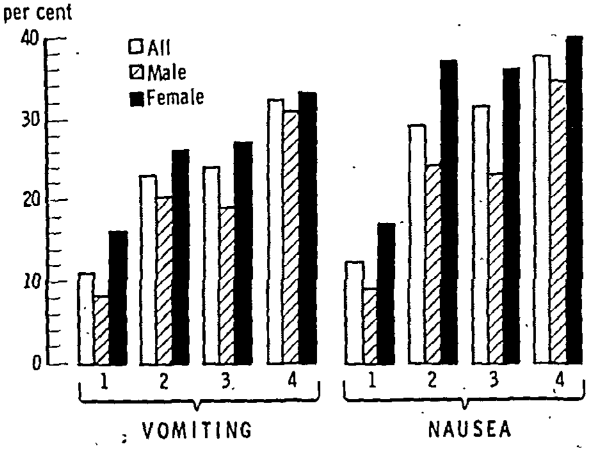
Results

Data concerning patients of age group 1 are included only in the general results (table 2), because we believe that the reactions of children should not be evaluated with those of adults. Results related to nausea are not reported in several tables for purposes of simplification; results concerning nausea always paralleled those obtained for vomiting.

Table 2.—*Incidence of Nausea and Vomiting in Relation to Age and Sex*

Age Groups, Yr.	Vomiting						Nausea					
	Total		M		F		Total		M		F	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Up to 10	54	35.5	34	33.6	20	40.0	57	38.0	36	35.4	21	42.0
11-17	29	45.3	22	50.0	7	35.0	32	50.0	23	52.2	9	45.0
18-49	168	26.9	45	23.0	123	28.6	214	32.7	53	27.3	161	37.4
50-65	97	20.0	37	14.8	60	25.0	112	23.2	39	15.6	73	31.7
Over 65	42	15.0	21	12.5	21	18.0	58	20.7	27	16.5	31	26.5
Total	390	24.3	159	21.0	231	27.2	473	29.5	178	23.7	295	34.5

There was a significant difference in the incidence of vomiting related to anesthetic agents (see figure); for males it was more pronounced than for females ($p<0.01$). The incidence of vomiting (table 2) varied significantly with age, especially in males ($p<0.01$). The incidence of vomiting in males was significantly different from that in females in patients over 11 years of age ($p<0.01$). The incidence of vomiting did not vary significantly with body type (table 3) in either the males or the females ($0.02<p<0.05$ for males; $0.2<p<0.3$ for females). The incidence of vomiting varied significantly with site of operation (table 4) for both sexes ($p<0.01$).



Vomiting and nausea in relation to anesthetic agent used. 1=thiopental and nitrous oxide combination, 2=ether, 3=cyclopropane, and 4=cyclopropane with ether.

There appeared to be a constant upward trend in the incidence of vomiting as the duration of the procedures increased (table 5), but the incidence was only of borderline significance ($0.01<p<0.02$).

TABLE 3.—*Distribution of Structural Types by Sex and Relation to Incidence of Vomiting*

Structural Type	Distribution				Incidence of Vomiting					
	Total		M	F	Total		M		F	
	No.	%			No.	%	No.	%	No.	%
Leptosome	516	35.5	214	302	103	20.0	31	14.4	72	23.5
Athletic	492	33.9	333	159	122	24.8	81	23.3	41	25.7
Pyknic	396	27.3	88	308	109	27.5	18	20.4	91	29 5

There was a significant relationship between the incidence of vomiting and the presence of a gastric tube ($p<0.01$). Among patients without gastric tubes the incidence was 25.3 and among those with tubes 15%. The incidence of vomiting with endotracheal intubation was 24.4 as against 22% without intubation. With the use of relaxants the incidence was 21.5 and without relaxants 24%.

Comment

A review of the pertinent literature shows that there has been a definite trend in recent years toward a lower incidence of postoperative nausea and vomiting after general anesthesia. Studies reported as recently as 1929 indicate an incidence well above 50 and sometimes as high as 80%.[4] In contrast, Dent and associates[5] reported a low percentage of 27.5 in 1955; Burtles and Peckett[6] 32 in 1957; and Bonica and associates[7] reported a percentage of 30.5 in 1958. Waters[8] reported 40.6% in his study of 1936 but only 35.5% in 1951. In our study the over-all incidences were 24.3% for vomiting and 29.5% for nausea (table 2). It should be pointed out that a number of patients emerged very rapidly from anesthesia, and that some of these patients may have vomited while still in the operating room or on their way to the recovery room. Had these cases been included in the results they would have increased the number of cases of vomiting reported in the recovery room by 15%.

TABLE 4.—*Incidence of Vomiting in Relation to Sex and Type of Surgery*

Site and Type of Operation	No. of Operations			Incidence of Vomiting					
				Total		M		F	
	Total	M	F	No.	%	No.	%	No.	%
Head and neck	135	52	83	44	32.6	14	26.9	30	36.0
Thyroid	37	4	33	17	46.0	4	100.0	13	39.4
Intrathoracic	43	23	20	9	21.0	3	13.0	6	30.0
Intra-abdominal ...	350	153	197	72	20.5	33	21.3	39	20.0
Biliary tract	97	28	69	22	22.6	10	35.7	12	17.3
Appendectomy ...	32	15	17	17	53.0	7	46.6	10	60.0
Gynecologic	189	...	189	59	31.2	...	....	59	31.2
Urologic	259	207	52	37	14.2	25	12.0	12	23.0
Peripheral	292	99	193	69	23.3	19	19.0	50	25.9

The anesthetic agent appears to be a factor of major importance in the incidence of postoperative nausea and vomiting (see figure). Results reported in the literature vary widely. Previous reports indicated an 80% incidence associated with diethyl ether anesthesia.[9] In more recent work the trend was lower and averages varied between 30 and 60%.[10] For cyclopropane the results vary between 24 and 50%.[11] Combined thiopental and nitrous oxide has always been reported as giving the lowest incidence, between 14.5 and 30%.[12]

The present study indicates that nausea and vomiting occur in 23.3% of patients receiving ether and in 24.1% of those receiving cyclopropane. The general belief that ether causes more nausea and vomiting than other inhaled anesthetic agents was not substantiated by the results. However, nausea and vomiting after anesthesia with ether are as a rule more persistent than after that with cyclopropane. The incidence after combined thiopental and nitrous oxide anesthesia (11%) was far lower than after any other agent.

The age of the patient (table 2) appeared to influence the incidence of postanesthetic vomiting, particularly in males; for both sexes, however, there was a definite tendency toward lower incidences among older patients. The sex of the patient is a factor of major importance. A higher incidence among females was observed in nearly all circumstances, regardless of the anesthetic agent used. Several other authors have made the same observation.[13]

TABLE 5.—*Incidence of Nausea and Vomiting in Relation to Sex and Duration of Anesthesia*

Duration of Anesthesia, Hr.	Patients, No.			Vomiting						Nausea					
				Total		M		F		Total		M		F	
	Total	M	F	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1 and under ..	408	153	255	77	18.8	24	15.6	53	20.7	104	25.0	28	18.3	76	30.0
1-2	479	249	230	104	21.6	44	17.6	60	26.0	132	27.5	48	19.2	84	36.5
2-3	287	123	164	72	25.0	28	22.7	44	27.0	90	31.0	32	26.0	58	35.3
3-4	172	74	98	51	30.0	18	24.3	33	33.6	61	35.4	22	30.0	39	39.8
Over 4	104	52	52	32	32.6	12	23.8	20	38.4	39	37.5	14	26.9	25	48.0

The site of operation (table 4) has an important role in the relative occurrence of emetic symptoms. This is a generally accepted observation; however, the respective influence of different types of surgery is a controversial subject, especially with respect to intra-abdominal operations.[14] Knapp and Beecher found little difference between intra-abdominal and other operations; Bonica and associates found a high incidence of vomiting after abdominal surgery; Burtles and Peckett found a relatively low incidence; and our results were very low. The divergence of these results obviously indicates that this complex problem is not solved.

Head and neck operations and particularly those on the thyroid were followed by a high incidence of emetic symptoms; this is in accord with the findings of other investigators.[15] The low incidence after operations on the urinary tract, also noted by Burtles and Peckett, is partly explained by the fact that the vast majority of patients undergoing this type of surgery are men over 50 years of age and partly by the fact that the thiopental and nitrous oxide combination was the anesthetic agent in 52% of the cases.

Several investigators have expressed the belief that the duration of a procedure could influence the incidence of postanesthetic nausea and vomiting.[10] Knapp and Beecher were unable to confirm this opinion. The results obtained in this study (table 5) appear to give some support to it. However, it is necessary before formulating a definite conclusion concerning the influence of duration of anesthesia to analyze certain factors which could bias the results. Different types of operations in relation to duration and age group did not appear to influence the findings. However, the various anesthetic agents do influence postoperative vomiting; consequently, it was important to correlate agent and duration. The distribution of agents used in anesthesias lasting one hour or less was as follows: combined thiopental and nitrous oxide, 135; ether, 28; cyclopropane, 206; and cyclopropane combined with ether, 35. The expected incidence of vomiting calculated for this distribution is 20%; this is very close to the 18.8% obtained in this study. The expected incidence for anesthesias lasting up to two hours is 22.5%; the result of this study showed it to be 21.6%. However, for the longer anesthesias the results were a little above the expected incidence; for anesthesias over three hours, 30 as against 26%, and for those over four hours, 32.6 as against 28%.

The important factor in the analysis is the fact that combined thiopental and nitrous oxide was used in 33% of the anesthesias of one hour's duration, in 22% of those of two hours' duration, in 9% of those of three hours' duration, in 5% of those of four hours' duration, and in only 1% of those lasting more than four hours. This relatively high percentage of thiopental and nitrous oxide anesthesia in the shorter procedures was a factor in the lower average incidence of emesis in these cases. The conclusion is that duration of anesthesia appears to have little influence on the incidence of nausea and vomiting; however, it should be noted that there is an upward trend in the incidence of vomiting as duration increases.

The concept that a gastric tube provides a beneficial effect is substantiated by the data of this study. This has also been the experience of several other investigators. The results in relation to endotracheal intubation and the use of relaxants indicate that these factors have no appreciable influence on postoperative vomiting.

Summary

Observations during the immediate postanesthesia phase were recorded in 1,602 patients. The over-all incidence of vomiting was 24.3%; the incidence in males was significantly different from that in females. The influence of body structure was not marked for either sex, but emesis was less frequent in the older age groups.

Anesthesia with use of combined thiopental and nitrous oxide was followed by vomiting in 11% of the cases. Ether and cyclopropane anesthesia were followed by vomiting in 23.3 and 24.1% of the cases respectively. The incidence of vomiting varied significantly with the site of operation for both sexes. The duration of anesthesia was not important in relation to postoperative nausea and vomiting, but there appeared to be an upward trend as duration increased. The gastric tube had a favorable effect, while endotracheal intubation and the use of relaxants had no appreciable influence on vomiting.

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AGRANULOCYTOSIS CAUSED BY PHENOTHIAZINE DERIVATIVES

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Agranulocytosis has sometimes followed the use of chlorpromazine and promazine, and there is reason to assume that it can also be induced by sufficient amounts of other drugs of the phenothiazine group. In most of the known cases this reaction occurred during the first 15 weeks of drug administration. In the cases here described two men, aged 72 and 41 years, had received chlorpromazine and promazine respectively; a third, aged 49, had received both drugs. At the height of the agranulocytosis the first patient had only 2% neutrophils and a total leukocyte count of 900 per cubic millimeter; in the other two patients the neutrophils vanished. Evidence in these cases indicated that the reactions represented individual idiosyncrasies to cumulative doses of the drugs and that fatalities can be prevented by sufficient alertness and prompt recognition of incipient neutropenia. The three patients recovered without signs of residual damage.

That a specific drug reaction could cause granulocytopenia was demonstrated in 1934 by Madison and Squier[1] and confirmed by Sturgis and Isaacs.[2] Both groups showed that small test doses of aminopyrine were the etiological agent in patients recovered from agranulocytic angina. The phenothiazine ring (see figure), containing sulfur and nitrogen, is toxic to bacteria, insects, and helminths; is present in a veterinary vermifuge; and is a constituent of the parent substance of thionine dyes such as methylene blue. In humans, phenothiazine induces hemolytic anemia, toxic hepatitis, skin irritation, and photosensitization. The first derivative which was found to be pharmacologically useful is chlorpromazine, which was introduced in 1952 in France. Its first trade name (Largactil) was designed to indicate its large action and many uses. This drug is similar structurally to promethazine (Phenergan) but lacks antihistaminic properties. At the present time, there are six other derivatives in use which have actions similar to chlorpromazine (see figure). Not included in this list are the most recent drug, trimeprazine (Temaril), which is similar to phenergan and has antihistaminic properties, and the tranquilizers thioridazine (Mellaril) and trifluoperazine (Stelazine). Reports since 1954 indicate that agranulocytosis is a side-effect of chlorpromazine therapy, and this reaction has also been noted with promazine, promethazine, prochlorperazine, perphenazine, and mepazine.

Chlorpromazine

A review of 58 cases from the literature and one case reported here provides the basis for some generalizations on the nature of agranulocytosis associated with chlorpromazine therapy. Reviews[3] provide information on 32 of the cases, and the remainder have been reported singly. The incidence of chlorpromazine agranulocytosis may be as high as three cases in 1,000 patients.[4] Data from 59 cases given in table 1 show the mean and the range. In most cases reported the patients had been given neuropsychiatric diagnoses; use of chlorpromazine in mental health institutions has undoubtedly influenced the reported mean age of 54 years (range

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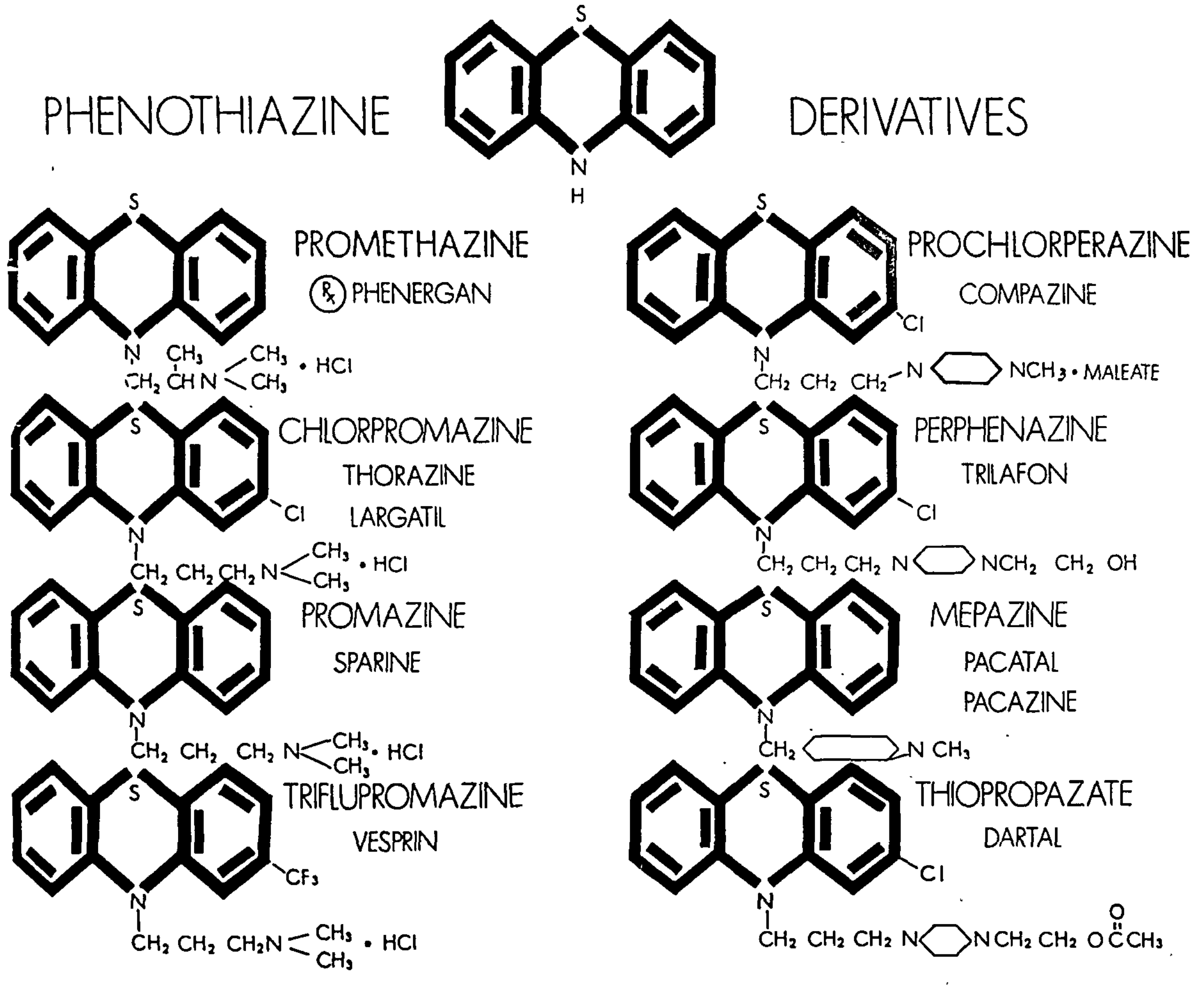
26 to 88 years). A great difference in sensitivity of patients is evidenced by the range of doses (from 1 to 52 Gm. [mean, 12.3]) of total drug administered on consecutive days prior to the reaction. The mean number of days of consecutive administration was 50 (range, 13 to 171), with a standard deviation of 26 days. This would suggest that two-thirds of the reactions can be expected to develop during the first 76 days and 95% during the first 15 weeks of drug administration. No other drug was administered concurrently in 35 cases, and chlorpromazine was the only phenothiazine derivative given in the remainder.



Of the entire group, 31 received hormone therapy in the form of ACTH, prednisone, or cortisone as well as antibiotics. The remainder received antibiotics alone. Steroid therapy did not seem to influence either mortality or recovery time. Twenty-two deaths with agranulocytosis were recorded. In general, about 10 days elapse after development of agranulocytosis and withdrawal of the drug before the leukocyte count returns to normal. The bone marrow "responds" (i. e., begins to recover) at least one week before the leukocyte count becomes normal. The time before return to normal or elevated total leukocyte levels has ranged in various reports from 5 to 16 days.

Promazine

Eleven cases plus one case here have been reported of agranulocytosis associated with promazine therapy.[5] Ages of patients and mean total dose are quite similar to those for chlorpromazine (table 1). From the experience in a few cases, it would appear that 95% of the reactions occur during the first 11 weeks of therapy. Three deaths have been reported, and the results of corticosteroid therapy and the recovery trends are also quite similar to those for chlorpromazine agranulocytosis. Bone marrow changes in cases of agranulocytosis after use of both these drugs are the same. Either there is almost complete absence of granulocytic elements or, if recovery has begun, there is predominance of progranulocytes or myelocytes. Erythropoiesis and thrombopoiesis have usually been reported as normal, except for approximately 16 cases in which the marrow findings were described as showing pancytopenia.

Other Derivatives

There is insufficient information on agranulocytic reactions to some of the other derivatives to permit any distinctions to be made. Mepazine agranulocytosis in four cases has followed a pattern similar to that of disease after chlorpromazine and promazine. A patient who had recovered from a reaction to chlorpromazine was shown to be sensitive to prochlorperazine and promazine.[3c]

Report of Cases

CASE 1.—A 72-year-old male was transferred on Sept. 22, 1957, from a mental institution to the Ann Arbor Veterans Administration Hospital with diagnoses of schizophrenia and acute appendicitis. Prior medication had included intermittent use of antibiotics, phenobarbital, reserpine, occasional injections of meperidine (Demerol), and intermittent injections of chlorpromazine during July and August, 1957. The patient had received chlorpromazine orally, 50 mg. four times a day intermittently from July 14, 1957, until his admission, for a total dose of 7.8 Gm. (table 2). Normal blood values were reported on July 15. Abdominal rigidity and tenderness in the right lower quadrant were present on admission, with 2 to 3+ pitting edema of both lower extremities. His temperature was 102 F (38.9 C). Blood values on admission were as follows: hemoglobin level, 13.5 Gm. per 100 cc.; hematocrit, 43.5%; leukocytes, 900 per cubic millimeter, with 2% neutrophils, 32% small lymphocytes, 58% large lymphocytes, and 2% plasmacytes; reticulocytes, 1%; and platelets, normal in number. His blood type was A negative, Rh positive. Appendectomy performed on the day of admission revealed a mucocele and atypical hyperplasia of the appendix mucosa without inflammation. Sternal marrow aspiration on Sept. 23 yielded a hypoplastic specimen with no mature granulocytic elements and only an occasional myelocyte. There appeared to be diminished erythropoiesis and number of megakaryocytes.

Inflammation of the pharynx developed, and rales were heard in the lower lung fields; he was treated with erythromycin, 1 million units of penicillin daily, and 1 Gm. of streptomycin daily. The febrile course continued from Sept. 22 through Sept. 30, when there was defervescence. Another sternal marrow examination on Sept. 26 revealed hypocellularity with rare occurrence of metamyelocytes and no over-all increase in myelopoiesis. The hemoglobin level was 12.2 Gm. per 100 cc. and leukocytes were 1,200 per cubic millimeter, with 5% neutrophils plus Türk's irritation cells. On Sept. 30 the leukocyte count was 5,250 and on Oct. 1, the day of defervescence, it was 11,200 per cubic millimeter, with 50% neutrophils. On Oct. 1, an aspirated specimen of sternal marrow was hypercellular, with marked increase in granulopoiesis and predominance of myelocytes. Use of antibiotics was discontinued, and the patient's recovery was uneventful. The leukocyte count continued to rise until Oct. 7, when it was 20,000 per cubic millimeter, with 82% neutrophils. It then gradually declined over the next 10 days to 9,000 to 10,000. Subsequently, the patient underwent transurethral resection of the prostate for benign hypertrophy. He received test doses of chlorpromazine (as shown in table 2) without significant reaction. The patient was last seen in January, 1958, when he was doing well, and his blood values were all within normal limits.

TABLE 1.—*Data from Case Reports of Agranulocytosis Caused by Phenothiazine Derivatives**

	Chlorpromazine	Promazine
Cases reported as of August, 1958, no.†	59	12
Age (mean), yr.	54(26-88)‡	57(46-74)
Mean total dose, Gm.	12.3(1.1-52.5)	14.4(2.8-37.0)
Consecutive days drug was given prior to reaction	50(13-171) S.D.§=26	41(14-83) S.D.=19
Deaths due to agranulocytosis	22	3
Steroid therapy, no. of patients	31	4
Recovered	19	2
Died	12	2
Days for response		
Steroid	10(5-16)	9(3-13)
No steroid	10(7-14)	11(8-13)

* Complete bibliography of all case reports will be supplied by the author on request.
† Includes cases reported in text.
‡ Range given in parentheses.
§ S.D.: standard deviation.

CASE 2.—A 41-year-old male with a diagnosis of schizophrenic reaction was transferred to this hospital on Oct. 14, 1957. Physical examination was within normal limits. Laboratory studies were normal, with 6,600 leukocytes per cubic millimeter and a hemoglobin level of 14.4 Gm. per 100 cc. On Nov. 12 it was noted that the patient had leukopenia and neutropenia and was febrile. He had received amobarbital (Amytal) and promazine, 250 mg. four times a day intermittently since Oct. 7, and meprobamate, 400 mg. intermittently. He received promazine, 200 mg. four times a day, from Oct. 15 to Nov. 12. A febrile toxic course followed, with pharyngeal ulceration, cervical adenitis with superficial ulceration, and severe sore throat with dysphagia. The lips and tongue were swollen, and the neck had the wooden-hard character of Ludwig's angina. His temperature ranged between 102.0 and 104.4 F (38.9 to 40.2 C). Treatment was with procaine penicillin, 600,000 units; streptomycin, 0.5 Gm., alternating with dihydrostreptomycin; benzathine penicillin G, 600,000 units by mouth; and oxytetracycline (Terramycin), 0.5 Gm. by mouth —all given every six hours.

Sternal aspirate on Nov. 12 was hypocellular, with no evidence of granulopoiesis and decreased numbers of erythropoietic elements and megakaryocytes.

Hemoglobin level was 10.8 Gm. per 100 cc. and hematocrit, 34%. The leukocyte count was 950 per cubic millimeter, with Türk's irritation cells and no neutrophils. The spleen was palpable, and there was a positive urine test for porphobilinogen (negative in a 1:10 dilution). This test was positive on Oct. 29, Oct. 30, and Nov. 1 but was not positive again on repeat determinations, including those at the time of test doses. On Nov. 15 the bone marrow was hypocellular, with normal erythropoiesis and thrombopoiesis. On Nov. 19 the bone marrow was more cellular, with progranulocytes and myelocytes, and the erythroid-myeloid ratio was 1:1. On Nov. 21 there was the first indication of granulopoietic response; leukocytes were 2,700 per cubic millimeter and the temperature abruptly became normal. On Nov. 22, the sternal marrow aspirate was very hypercellular, with increase in granulopoiesis. The leukocyte count continued to rise to a peak of 35,000 per cubic millimeter on Nov. 26, with 10% myelocytes, 22% metamyelocytes, and 29% nonsegmented and 25% mature neutrophils; increased platelets; and 1.5 to 2% reticulocytes. The hematocrit was 42%. Serum protein values and liver function test results were all normal.

Table 2.—*Observations in Two Cases at Onset of Therapy, During Agranulocytosis and Recovery, and During Drug Readministration*

	Onset of Therapy	After Stopping Therapy				During Drug Readministration			
Case 1—Chlorpromazine Agranulocytosis									
Date	7/15/57	9/23	9/26	9/30	10/7	11/5	11/20	12/13	
Fever	0	+	+	+	0	0	0	0	
WBC	7,400	900	1,200	5,250	20,000	11,900	9,100	8,350	
Neutrophils, %	45	2	5	51	82	63	70	57	
Hematocrit, %	46	18	41	44	44	36	35	38	
Dose, Gm.	Daily 0.2	Total 7.8	0	0	0	0.025	0.050	0.300	
Case 2—Promazine Agranulocytosis									
Date	10/15/57	11/12	11/20	11/26		12/13	12/16	2/23/58	2/27
Fever	0	+	+	0		0	0	0	0
WBC	6,600	950	1,000	35,000		7,800	7,300	10,000	6,750
Neutrophils, %	80	0	0	86		64	65	77	74
Hematocrit, %	43	34	35	42		43	44	47	46
Dose, Gm.	Daily 0.8	Total 23.2	0	0		0.025	0.050	0	0.3

During the toxic course, the ulcerating lesions did not show evidence of pus formation but cleared up promptly after Nov. 21. The spleen regressed. The patient was later given a week's course of meprobamate, 400 mg. daily, without reaction and was given test doses of promazine without significant reaction (table 2), except that after the 50-mg. test dose he developed a slight rash over his forehead. He received 25 mg. of promazine on Dec. 13 and 50 mg. on Dec. 16, with slight increase in temperature to 99.2 F (37.3 C) and no change in any blood value except for the fact that the percentage of eosinophils increased to 13. The patient was readmitted to the hospital in February, 1958, at which time he received further test doses of the drug without reaction (table 2).

Case 3.—A 49-year-old male was admitted to the Neuropsychiatric Institute on May 25, 1957, because of a diagnosis of schizophrenic reaction. Two years previously he had had an episode of jaundice after chlorpromazine therapy. The leukocyte count was 5,700 per cubic millimeter and the hemoglobin level, 14.9 Gm. per 100 cc. Promazine, 50 mg. four times a day, was administered on admission and the dosage was increased gradually to 250 mg. four times a day. A total of 10.3 Gm. of promazine was given over a period of 18 days. Other drugs given included methylphenidate (Ritalin), digitalis, and mercaptomerin (Thiomerin). The patient was transferred to the medical service on the 18th hospital day with a tentative diagnosis of impending thyroid storm, temperature of 102 F, and tachycardia.

At the time of transfer, there were 1,300 leukocytes per cubic millimeter, without neutrophils. Sternal marrow aspiration revealed normal megakaryocytes, no evidence of granulopoiesis, normoblastic erythropoiesis, and numerous plasmacytes. Use of promazine was discontinued, and antibiotic therapy with penicillin, streptomycin, nystatin (Mycostatin), and novobiocin was instituted. Hydrocortisone therapy was started on June 18 in a dosage of 200 mg. per day. The patient remained febrile (temperature from 99 to 105.6 F [37.2 to 40.8 C]) until June 23, when his temperature became normal. During this acute episode he became jaundiced. The total bilirubin level reached a peak of 11.2 mg. per 100 cc. (5.6 mg. direct) on June 18, 1957, and cleared rapidly thereafter. The leukocyte count on June 25 was 22,600 per cubic millimeter, with 82% granulocytes, including immature forms. Repeat marrow aspiration, done on June 26, showed a striking increase in granulocytic elements, with an erythroid-myeloid ratio of 1:9, all stages of granulocytic development, and a relative increase in myelocytes. The subsequent course of this patient was complicated by the development of an abscess of the forearm and of empyema with bronchopleural fistula. Coagulase-positive hemolytic Staphylococcus aureus was cultured from both of these infectious processes. The infections cleared after surgical drainage. The hemoglobin level on Sept. 6 was 10.3 Gm. per 100 cc., and leukocytes were 5,000 per cubic millimeter.

Comment

The mechanism of agranulocytosis produced by phenothiazine-derivative drugs appears to follow a definite pattern. In a patient[6] who had developed a reaction to chlorpromazine, the drug was readministered at 10-mg. and 25-mg. doses without effect, and the blood reaction was then reproduced after 1.3 Gm. given over a 13-day period. Small doses will not reproduce a reaction.[7] Table 2 demonstrates the course of the agranulocytosis in two of our patients and negative results by readministration of small amounts of the drug. This is not the type of result which one would expect if a highly sensitive immunological mechanism were responsible, as is the case with reactions to aminopyrine. Attempts have been made to demonstrate leukoagglutinins in phenothiazine agranulocytosis[8] without success. In case 2, leukoagglutinins were sought by adding the patient's serum taken during the height of the agranulocytic action to normal leukocytes in the presence of a small amount of promazine. No leukoagglutination over that of the mixture of normal serum and normal leukocytes could be demonstrated. It would appear that this type of reaction is a drug idiosyncrasy or cumulative toxicity in which large doses of the drug given consecutively over a period of days produce bone marrow depression which is initially manifested in the granulocytic series. This reaction can be reproduced in the same person by giving a comparable dose of the drug again. It may be that agranulocytosis would recur if phenothiazine derivatives were given to a person who had developed a reaction after administration of one of these compounds. These drugs should probably be classified as agents occasionally associated with the occurrence of granulocytopenia, as suggested by Wintrobe and Cartwright.[9] It is interesting to note that jaundice and agranulocytosis do not very often appear concurrently.

The efficacy of steroid therapy in this form of agranulocytosis is debatable. The usefulness of corticotropin and cortisone in some blood disorders, especially those associated with continuing immune reactions, is well recognized.[10] However, the beneficial effects of these hormones in drug-induced agranulocytosis appear not to be well established. Adrenal cortex stimulation induces eosinopenia and neutrophil leukocytosis and evidence of erythrocytic proliferations. This is not constant or prolonged, except for the eosinopenia; the values revert to normal after use of adrenal cortical hormones is stopped.[11] A review of case reports suggesting beneficial effects of steroid therapy reveals that, after the recognition of the leukopenia and stopping of the use of the drug, evidence of bone marrow response appeared after 7 to 10 days, which is the same time range as that for those patients who did not receive steroids. The same pattern has been noted in case reports of agranulocytic reactions to drugs other than phenothiazine derivatives. The question has been raised[12] as to whether corticosteroid therapy is indicated. It may be argued that adequate antibiotic coverage and supportive care during a period of agranulocytosis should be sufficient therapy and that the administration of steroids might suppress a much needed immune response. The tabulation in table 1 of deaths due to agranulocytosis after the use of phenothiazine derivatives affords no argument either for or against the use of steroids. Experimental observations would indicate that steroids do not have a beneficial effect on the bone marrow after myeloid depression. It was noted in animals that after irradiation[13] the administration of cortisone had an adverse effect on bone marrow regeneration. It has been reported[14] that the leukopenia induced by nitrogen mustard administration can be increased by cortisone.

Splenomegaly was noted in case 2 and in several of the cases previously reported. The enlargement occurred during the period of agranulocytosis and disappeared on recovery. Splenomegaly may represent a reticuloendothelial and lymphoid reactive hyperplasia during the period of agranulocytosis.

Summary and Conclusions

The phenothiazine derivatives in general use at the present time include chlorpromazine, promazine, mepazine, promethazine, prochlorperazine, perphenazine, triflupromazine, thiopropazate, and trimeprazine. Agranulocytosis appears to be a definitely established reaction to chlorpromazine and promazine, and there are indications that other phenothiazine derivatives may have this potential action.

Most of the reactions appear to occur within the first 15 weeks of consecutive administration. If the agranulocytosis is recognized promptly, patients recover completely, usually about 10 days after use of the drug is stopped. Antibiotics, but probably not corticosteroids, should be administered.

The reaction appears to be an individual idiosyncrasy to a cumulative toxic dose of the drug. Cross sensitivity to other phenothiazine derivatives appears to be likely in the case of persons who have had agranulocytosis after the administration of one of these compounds. Readministration of small test doses does not result in a reaction, and leukoagglutinins have not been demonstrated.

Awareness and recognition of this drug reaction and familiarity with the various phenothiazine derivatives should prevent fatal reactions from developing in the future. Recovery appears to be complete and without residual bone marrow abnormality.

Dr. R. C. Bishop, University of Michigan Medical Center, provided the data and observations in case 3.

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CLINICAL NOTES

SULFHEMOGLOBINEMIA DUE TO ACETOPHENETIDIN

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and
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The observation of cyanosis in a patient without findings of respiratory or cardiovascular disease or polycythemia vera leads one to consider as its cause the presence of an altered hemoglobin.[1] Although 5.0 Gm. of reduced hemoglobin is usually necessary to produce cyanosis, only 1.5 Gm. of methemoglobin or 0.5 Gm. of sulfmethemoglobin will cause detectable cyanosis.[2]

Once sulfhemoglobinemia or methemoglobinemia is suspected, spectrometric examination of the blood will confirm this diagnosis. However, at this point the sometimes difficult task of finding the offending agent begins, for numerous drugs have been incriminated, the most common of which are nitrates, sulfonamides, and aniline derivatives.[3] The following case history is illustrative of this problem.

Report of a Case

A 37-year-old woman, an interior decorator, was admitted to the hospital for the third time with a complaint of recurrent spells of weakness. For the past several years she had had spells of weakness which recently became more pronounced and were associated with increasing fatigue and lethargy. A few months prior to this admission she had completed a full-term pregnancy complicated only by low back pain. During the two months preceding her hospitalization, she had recurrent nonspecific low back pain. For relief she took up to 10 tablets daily of Daprisal and about 10 tablets daily of either Empirin compound or Bufferin. No history of ingestion of any other drugs was elicited. She was not exposed to heavy metals, other than paints. The family history and her own history were noncontributory. Review of systems revealed no cardiorespiratory or gastrointestinal symptoms.

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Examination revealed an extremely lethargic, well-developed, well-nourished young woman. Her skin, lips, and nailbeds were a peculiar ashen-gray color. Her pulse rate was 66 per minute, respirations 20 per minute, blood pressure 110/60 mm. Hg, and temperature 98.6 F (37 C). The chest was clear. There was no cardiac enlargement or murmurs. The liver and spleen were not palpable. Edema was absent. Reflexes were equal and active, and no sensory loss or muscle weakness was detected. Psychiatric evaluation revealed a subsiding reactive depression.

Laboratory findings showed a hemoglobin level of 12.3 Gm.%; hematocrit value 39%; mean corpuscular hemoglobin concentration 32%; white blood cell count 6,250 per cubic millimeter, with 75% neutrophils (74% polymorphonuclear cells, 1% stab forms), 23% lymphocytes, 2% monocytes; platelets adequate; red blood cell morphology unremarkable; sulfmethemoglobin 0.8 Gm.%; methemoglobin absent. Results of urinalysis were negative; urine coproporphyrin, trace, and no uroporphyrin or porphobilinogen. X-rays of the chest, skull, and wrists were not remarkable. An electrocardiogram showed inverted T waves in leads aVR and aVL and V_1, a deep Q wave in aVL, and a low R wave in V_1 to V_6.

The patient's course was uneventful and afebrile. All drug therapy was stopped. Five cubic centimeters of 1% methylene blue given intravenously had no effect on the cyanosis. Her depression lifted, and she was discharged with decreasing cyanosis. In six weeks the cyanosis had disappeared completely.

Comment

The identification of the altered hemoglobin level is relatively easy and is of importance in deciding the form of therapy to be undertaken.[4] The level of sulfmethemoglobin (0.8 Gm.%) was found by analysis to exceed the minimum level (0.5 Gm.%) necessary for the production of cyanosis.

Although the exact chemical nature of sulfmethemoglobin is unknown, it is thought that an atom of sulfur is introduced into the hemoglobin molecule and that there is a change in the globin linkage with heme.[5] This compound has a characteristic absorption band at 618μ. Methemoglobin has a band at 630μ. Sulfmethemoglobin has a brownish color which, unlike the brownish color of methemoglobin, does not become red on standing or after bubbling oxygen through it. Further, the absorption band of methemoglobin disappears after the addition of a few drops of 5% potassium cyanide to the solution.[2]

It is felt that the etiological agent responsible for the ashen-gray cyanosis in this case was the acetophenetidin present in the drugs that the patient had ingested for relief of her "arthritic pains." Daprisal contains 0.16 Gm. of acetophenetidin, 0.16 Gm. of acetylsalicylic acid, 0.032 Gm. of amobarbital, and 0.005 Gm. of dextro amphetamine sulfate; Empirin compound contains 0.16 Gm. of acetophenetidin, 0.23 Gm. of acetylsalicylic acid, and 0.03 Gm. of caffeine; and Bufferin contains 0.325 Gm. of acetylsalicylic acid, 0.05 Gm. of aluminum glycinate, and 0.10 Gm. of magnesium carbonate but no acetophenetidin. This patient had a daily intake of up to 3.2 Gm. of acetophenetidin over a two-month period, or a total intake of about 192 Gm. of acetophenetidin.

In previous reports the acetanilid in Bromo-seltzer and other preparations was the etiological agent most commonly incriminated.[6] In 11 cases in the recent literature, the acetophenetidin contained in proprietary drugs has been implicated as the cause of sulfhemoglobinemia.[7]

Both acetophenetidin and acetanilid have similar metabolic pathways.[3a] When given with sulfur, these drugs produce sulfhemoglobinemia in rabbits and dogs.[8] Frequently, in cases of cyanosis secondary to sulfhemoglobinemia, the patients are constipated, and it is postulated that a source of sulfur from the intestine is partially responsible. The rare case of enterogenous sulfhemoglobinemia is thought to be caused by such a mechanism. In our patient there was no constipation, nor were sulfur-containing drugs being administered.

The presence of anemia in patients with sulfhemoglobinemia is inconstant.[9] In most of the previously reported cases, anemia was not a feature or, if present, was secondary to some other factor. Careful studies have shown that once sulfmethemoglobin is in a cell it remains there for the life of that cell. The life span of these cells is normal.[8] Neither methemoglobin nor sulfmethemoglobin is a toxic substance; they produce toxic symptoms by causing anoxia that results from the reduced oxygen capacity of hemoglobin so altered.[2]

While intravenously given methylene blue abolishes acquired methemoglobinemia, there is no satisfactory therapy for sulfhemoglobinemia except withdrawal of the offending drug.

Summary

A case of sulfhemoglobinemia with cyanosis was caused by acetophenetidin. Physicians should be alerted to the dangers of this agent, which is present in many proprietary drugs used by the general public and the profession.

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HYPOKALEMIC MUSCLE PARALYSIS ASSOCIATED WITH ADMINISTRATION OF CHLOROTHIAZIDE

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Chlorothiazide is a new orally given diuretic whose potency equals that of the parenterally given mercurial diuretics.[1] While in vitro it appears to be a carbonic anhydrase inhibitor, the latter effect is not strikingly evident in vivo.[2] It acts directly on the renal tubules [3] in a manner similar to that of the mercurial diuretics.[4] The result is an increased excretion of sodium, potassium, and chloride in the urine, accompanied by diuresis.

The side-effects do not appear to be troublesome.[5] Among those reported are (1) gastrointestinal disturbances, including nausea, vomiting, abdominal cramps, and epigastric distress; (2) hemorrhagic manifestations in which patients exhibited hematuria and petechiae without changes in the clotting mechanism; and (3) an exaggeration of epilepsy due to systemic alkalosis.[5a] Wilkins [5b] has reported sexual impotence as a complication of chlorothiazide therapy and Drerup and co-workers [6] treated a patient who developed jaundice with pathological evidence of bile stasis while receiving the medicament. Transient skin rashes have also been reported,[3] as have hyperglycemia and glycosuria.[1] A clinical picture of impending hepatic coma [7] and ammonia intoxication [8] in patients with liver disease who were treated with chlorothiazide has also been observed.

Hypokalemia is the most important side-effect.[9] It is noted in 40% of patients receiving chlorothiazide without supplemental potassium.[1] In half of these cases the serum potassium level falls below 3.5 mEq. per liter [5b] and may be accompanied by weakness and trembling. Caution has been urged in the use of chlorothiazide in patients with renal [5c] and cardiac disease.[10] Lowering of the serum potassium level predisposes patients with heart disease to cardiac arrhythmias and digitalis toxicity.[5c] This is particularly liable to occur if such patients are placed on a low-sodium diet, for in this situation there is an increased excretion of potassium by the kidney due to the unavailability of sodium.

A patient who was recently treated with chlorothiazide developed a marked hypokalemia accompanied by selective muscle paralysis. The latter responded dramatically to the administration of potassium. Dr. Gibson, director of medical research of Merck Sharp & Dohme, stated that according to the information available to him this case is the first instance in which the serum potassium level had dropped so low and muscle paralysis occurred while chlorothiazide was being administered.[11] The uniqueness of this case merits its publication.

Report of a Case

A 60-year-old man was referred for medical evaluation because his ophthalmologist told him that there were "signs of high blood pressure in the eyes." When first seen on Dec. 4, 1958, he had no other complaints. His history was noncontributory, including no personal or familial episodes of periodic paralysis. Findings of the initial physical examination were within normal limits except for overweight (height 5 ft. 7 in. [170.2 cm.], weight 201 lb. [91.2 kg.]) and hypertension (blood pressure 180/124 mm. Hg). Funduscopic examination revealed some arteriolar constriction. Hemoglobin concentration was 12.5 Gm.%. Urinalysis revealed a specific gravity of 1.010; no albumin or sugar was present; and microscopic examination showed an occasional red blood cell and white blood cell per high-power field. Therapy at that time consisted of a 1,200 calorie diet and 250 mg. of chlorothiazide to be taken twice daily. The patient was instructed to return in two weeks.

On Dec. 19 when he was seen again he stated that he felt well but that he had not followed the diet. His weight at that time was 212 lb. (96.1 kg.)

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and blood pressure 190/80 mm. Hg. The patient was again advised about the necessity of following a low-calorie diet, and because the systolic pressure was still moderately elevated the chlorothiazide dosage was increased to 500 mg. twice daily.

During two subsequent visits on Dec. 29, 1958, and Feb. 6, 1959, his weights were 205 and 206 lb. (93.0 and 93.4 kg.). The blood pressure recordings were 170/95 and 165/90 mm. Hg. He felt well and stated that following the diet consisted in avoiding starchy foods. The chlorothiazide therapy was continued and dextro amphetamine was added at the last visit to aid him in curbing his appetite.

On March 2 he was seen at home because for the past two days he had been unable to bend his left thigh and raise his right arm. He added that one week prior to the onset of these symptoms he had noted a similar weakness in his right lower extremity. This lasted for two days and then cleared spontaneously. He had continued to take the chlorothiazide up to the time of examination. Physical examination revealed a complete inability on the part of the patient to flex his left thigh and to abduct his right arm. There were no sensory disturbances and the reflexes were normal. No pathological reflexes could be elicited and there was no weakness of any other muscle group. There was no elevation of the temperature or nuchal rigidity.

Serum Electrolyte Studies and Potassium Chloride Administration

	March											April
Serum Electrolytes, mEq./Liter	2	3		4	5*	6	7	8	9	10	11	3
Potassium	1.65	1.65†	2.15‡	2.8	2.95	3.6	3.9		5.05	5.1	5.5	4.8
Sodium					151.0 (repeated)		141.0		141.0	137.0	135.0	136.0
Chloride							102.0		106.0	109.5		109.0
HCO_3							27.7		25.6			
Potassium chloride administration		40 mEq. I.V. + 2 Gm. orally		2 Gm. q.i.d.	2 Gm. q.i.d.	2 Gm. t.i.d.	2 Gm. t.i.d.	2 Gm. t.i.d.	2 Gm. t.i.d.			

* Muscle paralysis no longer present.
† Before I.V. administration of potassium chloride.
‡ After I.V. administration of potassium chloride.

The patient was immediately hospitalized at University Hospital, where results of an initial complete blood cell count and urinalysis were essentially normal. A spinal tap done on admission (with difficulty) revealed an initial pressure of 270 mm. H_2O. The fluid was clear and contained nine white blood cells per cubic millimeter. Result of the Pandy test was slightly positive, and that of the Kolmer test was negative. Results of trichinosis complement-fixation and flocculation tests of the serum were negative. Neutralization studies on stool and cerebrospinal fluid specimens were negative for poliomyelitis, Coxsackie, and enteric cytopathogenic human orphan (ECHO) viruses.

Serum potassium level determined on the day of admission was 1.65 mEq. per liter. Because of the exceptionally low level the determination was repeated the following day and an identical result was obtained. It was then felt that the hypokalemia was secondary to the administration of chlorothiazide and was also responsible for the patient's symptoms. An electrocardiogram done at that time showed widening of the QRS complex with depressed S-T segments, and widened, inverted T waves fusing with prominent, upright U waves—all compatible with hypokalemia. On March 3 an intravenous infusion of 40 mEq. of potassium chloride was given, and immediately afterward the serum potassium level was 2.15 mEq. per liter. At this time the patient stated that the involved extremities felt somewhat stronger. However, a clinical examination failed to demonstrate any change. The patient was given 2 Gm. of potassium chloride by mouth that evening. The next morning the serum potassium level was 2.8 mEq. per liter and his general condition was unchanged. He was then started on therapy with potassium chloride, 2 Gm. four times daily. The morning of March 5 he awoke with full use of the affected extremities. His serum potassium level at that time was 2.95 mEq. per liter. The next day the potassium chloride dosage was reduced to 6 Gm. daily and was continued until March 10.

On March 5 the patient's serum sodium level was found to be elevated (see table) on successive determinations. Because of the possibility that aldosteronism might be present the salivary potassium level, which is characteristically elevated in this condition,[12] was determined on March 10 and found to be 21 mEq. per liter, which appeared to be within normal limits.[13] These tests, subsequent electrolyte studies, and the lack of resistance to therapy ruled out the diagnosis of aldosteronism. The patient was discharged from the hospital on March 11, feeling perfectly well. He was seen in April, at which time there was no evidence of recurrence of muscle paralysis, and his serum electrolyte levels were normal.

Summary and Conclusions

A patient developed muscle paralysis subsequent to hypokalemia during the administration of chlorothiazide. The marked drop in the serum potassium level and the clinical symptomatology were unusual; this appears to be the first such case reported.

The elevation of the serum sodium level accompanying this marked decrease in serum potassium is a change similar to that seen in aldosteronism. Perhaps, as has been previously suggested,[1] chlorothiazide in some way exerts its pharmacological action through the activation of aldosterone.

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HEPATIC DAMAGE DURING CHLORPROPAMIDE THERAPY

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Recently a new arylsulfonylurea, chlorpropamide (Diabinese), has been released for the management of diabetes mellitus. Its mode of action is similar to that of other sulfonylureas, but it has a more potent hypoglycemic effect than tolbutamide and is excreted more slowly. As a result, lower dosages may be used and a fairly constant blood level obtained. Studies of acute and chronic conditions in animals have shown that this drug possesses a low order of toxicity.[1] Clinical trial in approximately 2,000 cases, for periods up to one year, indicates that in some patients hepatic function tests may show transient deviations from the normal. In general these abnormalities have not been indicative of serious hepatic dysfunction and have reverted to normal even when the drug therapy was not discontinued. In eight cases jaundice appeared, sometimes associated with a skin rash and eosinophilia. These cases have all occurred within two to five weeks of beginning therapy and have been characterized by an elevation of the alkaline phosphatase level and by the presence of intracanalicular biliary stasis. When chlorpropamide therapy was discontinued, the jaundice disappeared and the liver reverted to normal.[1a] It is the purpose of this communication to report three additional cases of liver injury which occurred in a series of 49 patients treated with chlorpropamide in a clinical trial of the drug at the diabetes clinic of the Bronx Hospital.

Report of Cases

CASE 1.—A 50-year-old woman had been known to have diabetes for 20 years. Her condition had been managed by diet and administration of 100 units of globin zinc insulin daily. In an effort to improve the degree and stability of her control, she was given in addition 1 Gm. of chlorpropamide per day. About three weeks later, she noted sensations of chill, weakness, and loss of appetite, followed in a few days by the discovery of dark urine, light stools, and rash on her trunk. With the passage of an additional week, by which time she had ingested a total of 27 Gm. of chlorpropamide, she noted jaundice. There was no pain, fever, nausea, or vomiting. Her history was negative for liver

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or biliary tract disease. Her alkaline phosphatase level, which had been 10 King-Armstrong units before the drug therapy was started and 11 King-Armstrong units after two weeks of therapy, was found to be 37 King-Armstrong units. The white blood cell count was 6,300 per cubic millimeter, with a differential of 59% segmented forms, 30% lymphocytes, 2% monocytes, and 9% eosinophils. She was hospitalized on Oct. 10, 1958, for further studies.

The findings of the physical examination were negative, except for the presence of jaundice, a diffuse macular eruption on the trunk, and a soft, tender liver edge 2 fingerbreadths below the costal margin. Laboratory data on admission included the following findings: the alkaline phosphatase level was 80 King-Armstrong units, the serum bilirubin level 8.9 mg.%, and the cholesterol level 630 mg.%, with 34% esters. The thymol turbidity was 1.6 units and the cephalin flocculation test negative. The hemoglobin level was 11.6 Gm.%, and the white blood cell count 7,600 per cubic millimeter, with 74% segmented forms, 20% lymphocytes, and 6% eosinophils. Platelets numbered 490,000 per cubic millimeter. Results of urinalysis were negative, except for the presence of bile. On Oct. 16, the serum bilirubin level reached a peak of 9.4 mg.%, the alkaline phosphatase level was 86 King-Armstrong units, and the serum cholesterol level 770 mg.%. By the time of the patient's discharge these values had fallen to a serum bilirubin level of 0.8 mg.%, an alkaline phosphatase level of 26 King-Armstrong units, and a serum cholesterol level of 262 mg.%, with 75% esters respectively. The cephalin flocculation and thymol turbidity remained normal. On two occasions the serum albumin level was 4.1 and 4.0 Gm.%, respectively, and that of serum globulin 2.6 and 2.3 Gm.% respectively. A needle biopsy of the liver, performed on Oct. 16, showed normal liver architecture. There was mild pigmentation of the Kupffer cells and slight capillary bile stasis. While a spotty inflammatory reaction in the portal tracts was noted, no inflammatory or degenerative changes were observed in the hepatic cells. A gallbladder series performed on Nov. 10 showed several negative shadows suggestive of gallstones. The patient remained afebrile throughout her hospital stay. The rash and eosinophilia cleared by the fifth hospital day. Her diabetes was controlled by means of a diet containing 150 Gm. of carbohydrates, 75 Gm. of proteins, and 80 Gm. of fats, and the administration of 80 units of NPH insulin daily. She was discharged on Nov. 14, 1958, and was still asymptomatic when seen for a follow-up examination in January, 1959.

Case 2.—A 67-year-old woman was referred on Nov. 5, 1958, for admission from the diabetes clinic of the Bronx Hospital because of a rise of her alkaline phosphatase level from 13 to 53 King-Armstrong units while on chlorpropamide therapy. The patient had been a known diabetic for one year and had not followed a prescribed diet or taken insulin. Six weeks prior to her admission to the diabetes clinic, on Sept. 26, she appeared at the outpatient department of the Bronx Hospital complaining of marked polyuria and polydipsia, with weakness. On that day therapy with chlorpropamide, 1 Gm. per day, was started, and she was placed on a 1,500-calorie diet. The alkaline phosphatase level, which was 13 King-Armstrong units on Oct. 15 (three weeks after the onset of treatment), rose to 53 King-Armstrong units on Oct. 29 (five weeks after the onset of treatment). She experienced no pain, nausea, or anorexia. Her history was negative for liver or biliary tract disease. Medication was discontinued on Oct. 29, after a total of 32 Gm. of chlorpropamide had been taken.

At the time of admission, Nov. 5, 1958, she appeared asymptomatic, afebrile, and comfortable. There was no jaundice. The only significant finding was a soft, nontender liver, palpable 1 fingerbreadth below the costal margin. The remainder of the findings of the physical examination were normal.

The patient was put on a 1,500-calorie diet without insulin therapy. On admission the hemoglobin level was 79% (Sahli method) or 11.4 Gm.%; the red blood cell count was 4,200,000 per cubic millimeter; the total leukocyte count was 9,000 per cubic millimeter, with a differential of 1% eosinophils, 61% segmented forms, 37% lymphocytes, and 1% monocytes; and platelets numbered 215,000 per cubic millimeter. A sulfobromophthalein test on Nov. 5 showed 14% retention at the end of 45 minutes. The prothrombin time was 88% of control on the same day. On Nov. 6, the second hospital day, the blood glucose level was 153 mg.%, the van den Bergh reaction negative, the serum bilirubin level 0.2 mg.%, and the urea nitrogen level 14 mg.%. The total serum protein level was 6.7 Gm.%, with an albumin level of 4.5 Gm.% and a globulin level of 2.2 Gm.%. The alkaline phosphatase level was 22 King-Armstrong units. The total cholesterol level was 304 mg.%, with 72 mg.% of the total as esters. The prothrombin time was 42% of control (Smith's method). The thymol turbidity was 0.7 units and cephalin flocculation was negative at the end of 24 and 48 hours respectively. The urine did not contain bile. A needle liver biopsy performed on Nov. 11 showed no abnormality of architecture. A fair number of hepatic cells showed hydropic nuclei and some showed hyperchromatic nuclei. The portal tracts were mildly infiltrated with round cells. There was no evidence of bile stasis. On Nov. 14 the alkaline phosphatase level was 18 King-Armstrong units, the serum bilirubin level 0.4 mg.%, and the sulfobromophthalein test showed 5% retention at the end of 45 minutes. A gallbladder series performed on Nov. 19 gave normal results. On Nov. 20, the alkaline phosphatase level was 15 King-Armstrong units, and the total cholesterol level was 211 mg.%. The patient remained asymptomatic throughout her hospital stay and was discharged on Nov. 25, 1958, with her condition well controlled by administration of 20 units of NPH insulin daily. At a follow-up examination in January, 1959, she was asymptomatic and appeared clinically well.

CASE 3.—A 57-year-old housewife had been known to have diabetes for nine years. The disease had been well controlled by diet and administration of NPH insulin 90 to 110 units daily. She was admitted to the Bronx Hospital on Nov. 10, 1958. On Oct. 10, one month prior to her admission, therapy with chlorpropamide, 0.5 Gm. per day, had been started, and the NPH insulin intake was reduced gradually to 70 units daily. On Oct. 25, two weeks after the onset of treatment, the patient noted malaise, vague abdominal pains, and epigastric discomfort. On Nov. 7, two weeks later and three days prior to admission, she noted a skin eruption, light stools, and dark urine. There was no pain, nausea, or vomiting, but mild anorexia was noted. Her history was negative for liver or biliary tract disease. She discontinued the chlorpropamide therapy, but continued to take 70 units of NPH insulin daily. The total amount of chlorpropamide taken was 12.5 Gm. On Nov. 10, jaundice appeared and she was hospitalized. Her alkaline phosphatase level, which had been 13 King-Armstrong units on Oct. 16, one week after the onset of treatment with chlorpropamide, had risen to 17 King-Armstrong units on Nov. 5.

Physical examination revealed a middle-aged, well-nourished, well-developed female, afebrile and in no distress. There was jaundice of the sclerae, skin, and mucus membranes. A soft, nontender liver was palpable 1 fingerbreadth under the costal margin, and a scanty macular pink rash was noted on the chest. The remainder of the findings of the physical examination were normal. The patient was kept on a diabetic diet of 1,500 calories and received 70 units of NPH insulin daily. No other medication was given. The blood chemistry on Nov. 11 revealed a glucose level of 211 mg.% and a urea nitrogen level of 16 mg.%. The prothrombin time was 100% of control (Smith's method). The erythrocyte sedimentation rate was 79 mm. at the end of one hour (Westergren). On the same day, the hemoglobin level was 78% (Sahli method) or 11.3 Gm.%, the total number of leukocytes 7,050 per cubic millimeter, with a differential count of 3% eosinophils, 53% segmented forms, 43% lymphocytes, and 1% monocytes. The results of urinalysis were negative, except for a trace of bile. Urobilinogen was present in a 1:1 dilution. On Nov. 14 the blood showed an alkaline phosphatase level of 78 King-Armstrong units, the van den Bergh reaction was direct, delayed, with a serum bilirubin level of 1.4 mg.%. The total serum protein level was 6.8 Gm.%, with the albumin level 4.1 Gm. and the globulin level 2.7 Gm. The total cholesterol level was 432 mg.%. Cephalin flocculation was negative in 24 and 48 hours, respectively, and thymol turbidity 1.5 units. The blood glucose level was 168 mg.%. By Nov. 14 the rash was no longer discernible and the jaundice barely perceptible. A needle liver biopsy performed on the second hospital day was reported as showing normal hepatic architecture, with intense infiltration of the portal tracts by acutely and chronically inflamed cells. Mild bile stasis was noted, as well as some vacuolization of a number of liver cells. On Nov. 18 the serum bilirubin level was 1.1 mg.% and the alkaline phosphatase level was 43 King-Armstrong units. The gallbladder series done on Nov. 19 showed no pathology. The patient signed out against advice on Nov. 20, 1958, and did not appear for a follow-up examination.

Comment

The benign course of the hepatic damage, the elevated alkaline phosphatase values, and the liver biopsies demonstrating bile stasis make the type of jaundice due to chlorpropamide therapy similar to that due to thorazine hydrochloride[2] or to methyl testosterone.[3] This variety of hepatic damage, which may or may not be accompanied by jaundice, is characterized by intracanalicular obstruction due to edema and cellular infiltration around the minute intrahepatic bile ducts. It is to be noted that the pathological findings revealed by liver biopsy may be minimal even with fairly high elevations of the levels of serum alkaline phosphatase or bilirubin. The latent period before the onset of jaundice (or rising alkaline phosphatase levels) and, in two of our cases, the prodromal symptoms and the accompanying rash and eosinophilia, suggest that hypersensitivity may be the mechanism involved. As in the case of thorazine hepatitis, this sensitivity apparently may disappear, since the drug therapy may be resumed at a later date without a recurrence of the untoward hepatic effects. This was not tried in any of our cases, but has been done many times with thorazine[4] and by Hamff and co-workers[5] with chlorpropamide without repetition of the jaundice.

In order to detect this type of reaction to chlorpropamide, the serum alkaline phosphatase level should be determined at weekly intervals at least during the first six weeks of its administration and use of the drug discontinued if the value rises above normal. In our experience to date, these cases have all occurred within one to six weeks after onset of therapy, and the jaundice is generally preceded by a rash. According to Shay and Siplet,[6] a rise in the level of serum alkaline phosphatase indicates hepatic sensitivity, which may be reversed by discontinuation of the drug therapy. Discontinuation of use of the drug was the only treatment employed in the cases presented. It is to be noted that the dosages employed in these cases, 0.5 to 1.0 Gm. daily, were larger than those currently being recommended by the manufacturer. Because of the slow excretion rate of chlorpropamide, initial dosage should be 0.25 to 0.5 Gm. daily. In occasional cases as little as 100 mg. daily can be used as a maintenance dosage.

Summary and Conclusions

Hepatic demage occurred in 3 out of 49 patients employed in a clinical trial of chlorpropamide (Diabinese) therapy. The jaundice which occurred in two of the three cases was demonstrated to be due to intracanalicular bile stasis. This could not be shown in the third case, where a sharp rise in the alkaline phosphatase level occurred without jaundice; but the elevation in the alkaline phosphatase level and the abnormal retention of sulfobromophthalein suggest that the same mechanism was operative. The pathology revealed by biopsy was minimal in all three cases and not as severe as the liver function abnormalities would have indicated. Complete recovery occurred in all. It is suggested that this reaction may occur more frequently when the dosage of chlorpropamide exceeds 0.5 Gm. daily. Its use should be monitored by periodic determinations of the alkaline phosphatase level for the first six weeks.

2021 Grand Concourse (53) (Dr. Brown).

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JAUNDICE OCCURRING DURING NICOTINIC ACID THERAPY FOR HYPERCHOLESTEREMIA

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The administration of nicotinic acid in dosage of 3 to 6 Gm. a day has proved to be an effective method of reducing serum cholesterol levels. Experience with this medication for periods up to three years has been reported from the Mayo and the Jackson clinics.[1] Except for a few patients in whom there has been a transient abnormality of cephalin-cholesterol flocculation or transaminase, no renal, hematopoietic, or liver abnormalities have been noted.[2] Sulfobromophthalein (Bromsulphalein) tests and liver biopsies have failed to indicate other evidences of toxicity.[3] However, a definite decrease in glucose tolerance with some glycosuria has been noted.[4]

This report is submitted in order to record a case of jaundice occurring during the administration of nicotinic acid and presumably due to intrahepatic cholestasis resulting from drug toxicity.

Report of a Case

A 23-year-old man was first referred to me in June, 1957, because of an abnormal serum cholesterol level of which he had been aware since he was 17 years of age. He had no symptoms. His mother had died at 40 years of age of a myocardial infarction; his only brother, aged 20, is also known to have a cholesterol abnormality.

Pertinent features of the physical examination revealed a well-appearing, 6 ft. (182.88 cm.), 132 lb. (59.9 kg.) male with dense arcus senilis and xanthomas in the extensor tendons of the fingers, in the Achilles tendons, and in the plantar fascia. An electrocardiogram revealed normal findings. Three serum cholesterol measurements varied from 300 to 350 mg.%.

A 30-Gm. animal fat diet was established, with 3 oz. (85.05 Gm.) of supplemental corn oil administered daily. The patient was not seen again until

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Assistant Clinical Professor of Medicine, Medical Center, University of California, Los Angeles.

October, 1957, at which time his cholesterol level was 373 mg.%. In December, 1957, the administration of nicotinic acid was begun, 1 Gm. three times a day after meals. The remainder of the events in his course, including the side-effects and the laboratory data, are depicted in the figure. It will be noted that there was a prompt decrease of the serum cholesterol level to 225 mg.%, and it was maintained at levels between 150 and 215 mg.% for 40 weeks. When the administration of nicotinic acid was discontinued because of severe itching, the serum cholesterol level quickly returned to more than 400 mg.% then fell sharply again with the reinstitution of nicotinic acid therapy. The decreasing size of one of the fascial xanthomas is depicted in the figure. During the 72nd week, when the patient was first noted to have jaundice and the medication was stopped, the only complaints were of itching and excessive sweating. His appetite and strength were normal and he was afebrile. The liver was palpable 4 cm. below the costal margin but was not tender. Laboratory studies disclosed bile-tinged urine with many granular and cellular casts, a few red blood cells, and no albumin. The complete blood count was normal. Liver function tests revealed a total serum bilirubin level of 7.4 mg.% with a one minute direct of 1 mg.%, alkaline phosphatase of 45 King-Armstrong units, thymol turbidity of 3.8 units, creatinine of 1.04 mg.%, fasting blood sugar level of 74 mg.%, and serum glutamic oxalacetic transaminase level of 91 units. Prothrombin time, reticulocyte count, serology, cephalin-cholesterol flocculation tests and heterophil agglutination time were normal. The patient was hospitalized. During a 20-day period the bilirubin, alkaline phosphatase, and transaminase levels and urinalysis returned to normal and the itching disappeared. The cholesterol also returned to pretreatment levels. No therapy was initiated other than rest and discontinuing the administration of nicotinic acid.

Comment

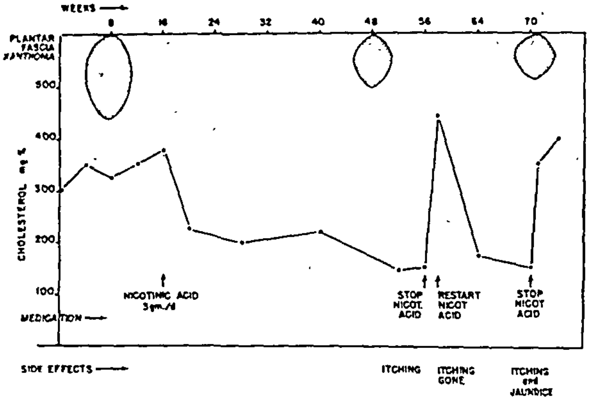
The rationale for the use of nicotinic acid and the physiological mechanisms for reducing serum cholesterol levels are only partially understood.[5] There is good reason to suspect, however, that there are alterations of the enzyme systems of the liver which are involved in cholesterol synthesis and conversion to bile acid.[6] It is conceivable that such alteration of liver activity could result in the kind of liver damage produced by methyl testosterone, chlorpromazine, and other drugs.[7]

Of the 18 other patients in our series currently taking nicotinic acid as a cholesterol depressing agent, no other serious toxic side-effects have been noted. One patient had transient glycosuria. In general there has been a gratifying decrease in serum cholesterol levels and relative concentration of beta-lipoprotein. Certainly in a disease such as familial hypercholesteremia, with its grave potential for early coronary disease, one is justified in using any relatively safe method to reduce serum cholesterol levels. Moreover, it may be possible to remove lipids from tissue deposits, since in this case there was demonstrable reduction in xanthoma size.

Summary

A patient with familial hypercholesteremia and tendon xanthomas exhibited marked reduction in serum cholesterol levels after therapy with large doses of nicotinic acid. The treatment was discontinued after 14 months because of the onset of jaundice, which probably represented intrahepatic cholestasis due to nicotinic acid toxicity.

Veterans Administration Center, Bldg. 114 (25).



Effect of nicotinic acid in large dosage on serum cholesterol levels.

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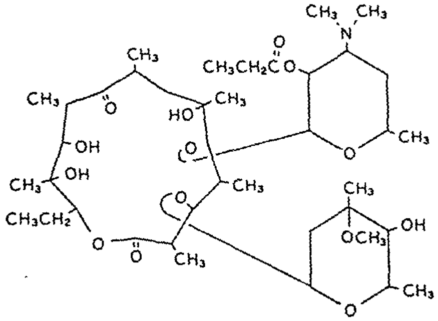
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Erythromycin Propionate (Ilosone).—Propionyl erythromycin ester.—The propionic acid ester of erythromycin. The structural formula of erythromycin may be represented as follows:



Actions and Uses.—Erythromycin propionate is active against the same pathogenic organisms and has the same uses as erythromycin free base. When administered orally, this ester produces an earlier onset of therapeutic blood levels than does the free base. Blood levels are also higher and of longer duration than those attained with like amounts of the free base. (See the monograph on erythromycin in New and Nonofficial Drugs.)

Dosage.—Erythromycin propionate is administered orally. The usual dose for adults ranges from 250 to 500 mg. every six hours, depending on the severity of the infection. For overwhelming infections, doses as high as 1 Gm. every six hours have been used. In such cases, however, institution of parenteral therapy should be considered. For children up to 50 lb. (22.7 kg.) of body weight, the usual daily dose is 125 mg. every six hours. Heavier children may receive the full adult dose.

Preparations.—capsules 125 mg. and 250 mg.

Year of introduction: 1958.

Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of erythromycin propionate.

Relaxin (Cervilaxin, Releasin).—A factor which produces relaxation of the pubic symphysis and dilation of the uterine cervix in certain animal species. It is a protein or polypeptide of relatively low molecular weight extracted from the ovaries of pregnant sows. Relaxin is assayed biologically.

Actions and Uses.—Relaxin is a naturally occurring substance which is produced by the corpus luteum during pregnancy. Increasing concentrations of relaxin can be detected in the blood and urine of animals and humans during the last two-thirds of the gestation period; it virtually disappears within 24 hours after delivery. The physiological function of relaxin during pregnancy is not known. When given to castrated, estrogen-primed guinea pigs, the drug causes a relaxation of the pubic symphysis. This effect, due to proliferation of capillaries and dissolution of collagen fibers, forms the basis for one of its biological assays. Relaxin has also been demonstrated to inhibit, both in vivo and in vitro, the contractions of uterine muscle in experimental animals. There is some evidence that it effects a relaxing or softening of the uterine cervix of pregnant laboratory animals and humans at term. The relationships, both chemical and physiological, between relaxin and lututrin are far from clear. However, the recent application of countercurrent distribution and chromatographic techniques would suggest the presence in the ovary of at least two distinct factors possessing uterine relaxation activity. One of these factors, relaxin, in addition to this effect on the uterus, also is capable of exerting a pronounced relaxing effect on the pubic symphysis. Since this latter effect is minimal with the second factor, it is conventional to reserve the term "uterine relaxing factor" for lututrin.

The ability of relaxin to inhibit uterine contractions has been demonstrated both in vivo and in vitro in experimental animals and humans. This inhibition is apparently not related to the mechanism of oxytocin stimulation, since the latter will restore uterine contractions even in the presence of relaxin. Further, tokodynamometer studies in humans have revealed a similar effect on uterine motility. Such experiments led to the introduction of relaxin as an agent designed to halt premature uterine contractions between the 29th and 36th week of pregnancy. The multiplicity of factors causing premature labor, the difficulty of identifying true labor, the lack of properly controlled series, and differences in dosage or route of administration of relaxin have all contributed to equivocal results in this indication.

The principal therapeutic interest of relaxin in obstetrics lies in its effects on the uterine cervix. As a result of favorable animal experiments, the drug has been proposed for clinical use as a "cervical softening" agent which is said to shorten the duration of full-term labor by facilitating cervical dilation. Although many clinical investigators believe that relaxin exerts a cervical softening effect, there is some disagreement as to its merits in the shortening of labor. On the basis of subjective observations, some obstetricians report that relaxin is effective in easing and shortening labor in the majority of patients, primiparas or multiparas, provided that the cervix is already effaced and dilated at least 2 to 3 cm. at the time the drug is given. Conversely, other investigators, employing more objective clinical methods, have been unable to detect any effect. Part of the confusion in this regard arises as a result of the frequent use of relaxin in conjunction with oxytocic agents for the elective induction of labor at term. However, it would appear from recent controlled experiments that the responsiveness of the uterus to either endogenous or exogenous oxytocin may contribute materially to the effects of relaxin on the uterus. If labor contractions are well established and at frequent and uniform intervals, the administration of relaxin may shorten the course of labor. On the other hand, the administration of the drug to a patient having desultory labor frequently results in a temporary cessation or slowing of the progress of labor. It should be kept in mind that the cervical softening effect of relaxin is of little help in dysfunctional labor or uterine inertia in which the ineffectiveness or weakness of myometrial contractions, and not the degree of cervical dilation, is the factor responsible for the impeded progress of labor. Hence, there seems to be little rationale for the use of relaxin alone in the induction of labor, since oxytocin is necessary to establish good uterine contractions. Its suitability for use in cases of so-called cervical dystocia must await the results of double-blind studies now in progress.

Relaxin has been proposed for use in the treatment of severe dysmenorrhea. The rationale for its use in this indication is based first on tokodynamometer studies, which demonstrate strong uterus motility inhibiting properties in dysmenorrheic patients, and secondly on the cervical softening effect, which has been compared to mechanical dilation of the cervix prior to the onset of catamenial flow that frequently provides relief of pain. Controlled studies now in progress may shed more light on the usefulness of the drug for this purpose.

Among the miscellaneous proposed uses of relaxin is its employment to aid in the expulsion of retained dead fetus and the prevention of hypofibrinogenemia. In one series of cases, the use of large doses of relaxin for cervical softening prior to the use of oxytocin for induction of labor was claimed to be of significance. However, confirmation of this observation in a controlled series is indicated.

One of the experimentally observed effects of relaxin in laboratory animals has been an increase in the elasticity of the skin. Hence, the drug has been tried clinically for the treatment of scleroderma. Some improvement, as evidenced by relief of vasospasm, healing of trophic ulcers, and increase in skin elasticity, has been reported by several authors. Such symptomatic improvement continues as long as relaxin is administered, but the patients usually regress when therapy is terminated.

Since relaxin is a pork protein, it can give rise to sensitivity reactions ranging in severity from chills after its intravenous administration to acute anaphylactoid shock. Although the latter severe reaction has been encountered only rarely, skin testing is advisable for all patients. Except for occasional allergic manifestations, no other side-effects or untoward reactions have been reported.

Dosage.—Relaxin is administered intravenously or intramuscularly. The product is presently assayed by two methods, both of which equate dosage in terms of milligrams. One assay utilizes a guinea pig unit (G. P. U.) which is defined as "that amount of relaxin which produces relaxation of the pubic symphysis in two thirds of a group of 12 or more guinea pigs." The mouse assay is also utilized. This consists of the direct measurement of the interpubic ligament in estrogen-primed immature mice. Since the assay procedures are not precise and the technique of assay varies, the comparative potency of commercial preparations has not been clearly elucidated.

At the present time, precise recommendations for dosage are not possible. However, for cervical softening in normal labor or in cases of cervical dystocia, the proposed doses range from 40 to 120 mg., administered by intravenous drip in 250 to 500 cc. of sterile diluent at rates varying from 4 to 8 cc. per minute. Alternatively, the drug has been injected intramuscularly in doses of 40 mg. every two hours for three doses.

When used in conjunction with oxytocic agents for the elective induction of labor, the drug is administered by intravenous drip after rupture of the membranes. The dosage is that outlined previously for normal labor.

Although the clinical evidence to support its efficacy in premature labor is equivocal, relaxin has been administered intramuscularly in doses of 40 mg., followed by 20 mg. every two hours. It has also been given intravenously in doses of 40 to 80 mg., in 1,000 cc. of 5% dextrose in water for injection at a rate of 4 cc. per minute.

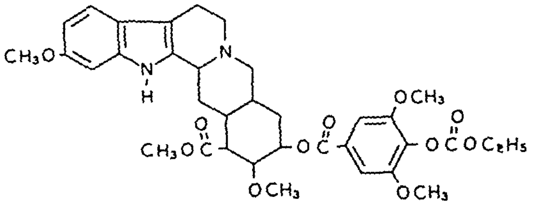
Proposed intramuscular doses for other claimed uses of relaxin are as follows: for dysmenorrhea, 20 mg. every four hours; for scleroderma, initially 20 mg. per day until therapeutic effects are known, followed by the lowest doses compatible with continued improvement; for delivery of retained dead fetus, 320 mg. in six doses over a period of 12 hours. Until more evidence of clinical efficacy appears in the literature, the foregoing proposed doses are considered experimental.

Preparations.—solution (injection) 20 mg. in 1 cc., 40 mg. in 2 cc.

Year of introduction: 1956.

The National Drug Company and Warner-Chilcott Laboratories, Division of Warner-Lambert Pharmaceutical Company, cooperated by furnishing scientific data to aid in the evaluation of relaxin.

Syrosingopine (Singoserp).—Carbethoxysyringoyl methyl reserpate.—Syrosingopine is prepared from reserpine by hydrolysis and reesterification. The structural formula of syrosingopine may be represented as follows:



Actions and Uses.—Syrosingopine is proposed for use as an antihypertensive agent and is closely related chemically to reserpine. (See the monograph on reserpine in New and Nonofficial Drugs.) When equal doses of the two drugs are compared, syrosingopine is both less potent and less toxic than reserpine. The two probably have about the same margin of safety.

Syrosingopine depresses the blood pressure in anesthetized and unanesthetized normotensive dogs, neurogenic hypertensive dogs, and in rats with adrenal regeneration hypertension. In dogs, the hypotensive effect is accompanied by a reduction in heart rate of 15 to 20%. It also reduces the rate of the isolated heart without altering the force of contraction or the coronary blood flow. It obtunds the carotid occlusion reflex.

Small doses of syrosingopine in dogs produce miosis, slight respiratory stimulation, and relaxation of the nictitating membrane. Larger doses produce sedation. It is one-twentieth as potent as reserpine in depressing the spontaneous activity of mice and one-tenth as potent in impairing the performance of monkeys in a discrimination learning task. Syrosingopine stimulates the secretion of hydrochloric acid in the denervated Heidenhain pouch of the dog but is less active in this respect than reserpine.

Clinically, syrosingopine alone is effective in some cases of mild or moderate labile hypertension. However, as is the case with all Rauwolfia compounds, syrosingopine generally will not provide satisfactory control of severe hypertension unless it is used in conjunction with more potent antihypertensive drugs. When given in combination with such agents, syrosingopine may make it possible to reduce their dosage.

Chronic toxicity studies in animals have disclosed no serious adverse effects on the bone marrow, liver, kidney, or other tissues. Side-effects reported in the clinical usage of the drug are similar to those of other Rauwolfia alkaloids. The most frequent of these is nasal congestion, followed closely in order of incidence by gastric complaints, drowsiness, and fatigue. Less frequently reported symptoms include headache, increased dreaming, emotional depression, and skin eruption.

To date, syrosingopine has been used only for the management of hypertension. Its advantages and limitations appear to be similar to those of other Rauwolfia drugs. Although early reports indicate that side-effects may be less troublesome than with other members of this group, a definitive assessment of the efficacy and toxicity of syrosingopine relative to the parent substance reserpine and other antihypertensive agents must await further clinical trial.

Dosage.—Syrosingopine is administered orally. The optimal dose (i. e., that which produces the best control of blood pressure without prohibitive side-effects) must be carefully determined for each patient. The suggested initial dose is 1 mg. per day. Since the effects of syrosingopine are manifested only slowly, it is advisable to maintain the initial dosage for a period of two weeks. Then, if there is inadequate clinical response, the daily dose may be gradually increased up to 3 mg. (in divided amounts), provided that each increase is maintained for a sufficient period to establish the level at which untoward effects appear. Occasionally, a patient may tolerate a higher daily dose.

Preparations.—tablets 1 mg.

Year of introduction: 1959.

Ciba Pharmaceutical Products, Inc., cooperated by furnishing scientific data to aid in the evaluation of syrosingopine.

REGRESSION OF DISEASES.—A communicable disease may spread throughout an area from one or more foci, and then gradually recede, even without effective treatment, until it is again confined to a few foci, or even disappears. Trachoma, for example, was brought into Europe by Napoleon's army on its return from Egypt, and ravaged the entire continent; but it has now practically disappeared from most European countries. Yaws has similarly almost disappeared from Ceylon, where in 1916-1920 there were 30,000 to 35,000 people with yaws lesions attending the outpatient departments of hospitals every year.—Yaws: Disease in Regression, *WHO Chronicle,* May, 1959.

COUNCIL ON FOODS AND NUTRITION

The Council has authorized publication of the following report.

Philip L. White, Sc.D., *Secretary.*

PROBLEM OF ANTIBIOTICS IN FOODS

Henry Welch, Ph.D., Washington, D. C.

In the United States antibiotics are probably our most important and most widely used therapeutic agents, and it is unlikely that any one of us will pass from "cradle to grave" without having one or more administered to us for some sound medical reason.

Background to the Problem

In 1957, total antibiotic production was over 2,500,000 lb., and it probably need not be emphasized here that these drugs have had wide and, in some cases, indiscriminate use. Their remarkable curative powers, more pronounced perhaps in the early days than now, resulted in their being injected, insufflated, given by mouth, spread on every part of the body, and sprayed intra-abdominally, intracisternally, intrapleurally, and intravaginally; no surface or cavity of the body has remained inviolate.

There are now over 400 preparations of antibiotics available for clinical use, and they run the gamut of injectables, ointments, powders, sprays, capsules, syrups, ear and eye drops, suppositories, troches, and tablets. Antibiotics have saved tens of thousands of lives in the past 15 years, and the reduction in the rates of mortality, morbidity, and complications of diseases has affected the lives of millions. Nevertheless, with such major advances in therapy and consequent wide use (not to mention indiscriminate use), unfortunately we have to face the accompanying untoward side-reactions that invariably follow. In the case of penicillin, a relatively atoxic drug, the "side-reaction" is its potentiality for sensitizing certain individuals. Although the other antibiotics are, in general, poor sensitizers, other side-reactions may occur after their administration. Thus, we have the initial provocation brought about by the extensive therapeutic and prophylactic use of a group of very valuable drugs.

Unfortunate Reactors

It is estimated that about 10% of the population in the United States has a tendency to become sensitive in the course of a lifetime to some food, drug, cosmetic, or other substance. Within this group of people there is a great variation in susceptibility to sensitization. Some acquire it easily, whereas others are more resistant. Some may be sensitive on first contact (the atopic group), while others require at least one contact, and still others may require several contacts before exhibiting a reaction. The reactions, too, vary in degree from mild, transient rashes to prolonged urticaria, and from a brief asthmatic attack to fatal anaphylactoid shock. Fortunately, these serious allergic manifestations occur less frequently in children to whom tons of antibiotics are administered yearly.

Since the population of the United States is estimated at over 175 million, we are concerned primarily with perhaps 17 to 20 million individuals who may react to contact with antibiotics—through proper therapeutic use or, inadvertently, through eating or drinking foods containing them. In the first case, the physician and patient have a choice, but in the latter instance there is none.

Introduction of Antibiotics in Foods

The extension of the uses of antibiotics to fields other than for prevention and treatment of human disease has magnified the problems of the physician from the standpoint of the side-reactions he may encounter in his daily practice.

Antibiotics are used in animal nutrition for promotion of growth in swine, chicks, and poults. Therapeutic and prophylactic use of large quantities of antibiotics is made for animals such as cows, beef cattle, swine, and chicks. These drugs are now being used as crop sprays to prevent blight in apples, pears, walnuts, and beans and to combat bacterial diseases of tobacco, tomatoes, peppers, and cherries. Two antibiotics, chlortetracycline and oxytetracycline, have been approved for use as preservatives on poultry and fish. A number of studies have been made to demonstrate their effectiveness as preservatives for vegetables, beef, ham, and other perishables.

The actual or potential introduction of antibiotics into the food supply poses the same problem as does the use of any other chemical. This grow-

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Director of Division of Antibiotics, Food and Drug Administration, U. S. Department of Health, Education, and Welfare.

ing use of chemicals in food is one of the most serious problems facing public health authorities today, increasing the complexity of diagnosis and treatment immeasurably. It should be emphasized, however, that the problem of contamination of foods with antibiotics is very small when compared with other potential chemical contaminants of food. There is virtually no limit to the expanding list of chemicals that may find their way into our food supply. Chemicals are promoted as stabilizers, preservatives, disinfectants, antioxidants, extenders, tenderizers, emulsifiers, growth promoters, fumigants, herbicides, defoliants, fungicides, miticides, bleaches, sweeteners, conditioners, colors, and flavors. In addition, food packages that incorporate new plastics, enamels, films, plasticizers, catalysts, and coatings are further potential sources of food adulteration.

Uses of Antibiotics

Animal Feed.—Antibiotics are used in animal feed for growth stimulation and for the prevention and treatment of disease. The quantities of antibiotics authorized by the Food and Drug Administration in such feeds range from 5 to 200 ppm. When these medicated feeds are used in the manner prescribed by the FDA, there are no drug residues in the meat, eggs, or milk of treated animals. Therefore, when such feeds are properly used, they do not constitute a public health hazard. However, there is always the possibility of misuse.

Crop Sprays.—Antibiotics used as crop sprays are dissipated before the edible portion of the plant is formed, and, since they do not reach the consumer, no public health problem is involved.

Food Preservation.—Extensive experiments have been conducted to explore the potentialities of antibiotics as food preservatives. In November, 1955, the FDA approved the use of chlortetracycline for the preservation of raw poultry. Approximately one year later similar approval was given for oxytetracycline. Tolerance levels for these drugs were established under the provisions of the Miller Pesticide Chemicals amendment to the federal Food, Drug, and Cosmetic Act, passed by the 83rd Congress in 1954. These drugs act as preservatives and extend the "shelf life" of the fowl. Under the Miller amendment, the applicant must demonstrate "usefulness" to the satisfaction of the United States Department of Agriculture and "safety" to the FDA.

The tolerance level in the raw bird for both chlortetracycline and oxytetracycline was established at 7 ppm in any part of the bird. (This is about 1.5 mg. per serving of a one-half pound.) However, before approval of this tolerance level was granted, it had to be shown that no antibiotic residues could be found in the poultry after cooking by broiling, frying, boiling, or baking. In April, 1959, a tolerance level of 5 ppm was established for chlortetracycline in certain kinds of raw fish and shellfish.

A considerable number of investigations of the usefulness of antibiotics in the preservation of meats also have been completed. However, approval of this use by the establishment of tolerance levels under the Miller amendment have not been granted as yet and can be obtained only when conclusive evidence is presented that such use is not detrimental to the health of the general public.

Indirect Antibiotic Adulteration of Milk

In addition to being directly introduced into the food supply, antibiotics also may find their way indirectly into foods. In 1948, it was noted that milk from cows treated for mastitis with penicillin by intramammary infusion often failed to produce a satisfactory cheese product. This was due to the inhibition of the starter culture used in cheese manufacture by the antibiotic present in the milk.

Realizing that antibiotics might also reach the consumer by way of milk, the FDA required that mastitis preparations carry a warning in their labeling to the effect that "milk from treated segments of udders should be discarded or used for purposes other than human consumption for at least 72 hours after the last treatment." In further recognition of the possibility that antibiotics might get into the food supply, a statement of policy was issued in February, 1953, by the Secretary of the U. S. Department of Health, Education, and Welfare concerning the direct or indirect addition of antibiotic drugs to foods for human consumption. In effect, the policy statement was as follows: "The presence of antibiotic drugs in foods intended for human consumption, or the direct or indirect addition of such drugs to such foods, may be deemed an adulteration within the meaning of section 402 of the Federal Food, Drug, and Cosmetic Act."

Very large amounts of antibiotics are used in the treatment of milk-producing cows infected with mastitis. It is estimated that more than 75 tons of these drugs is used yearly in the treatment of this widespread infection. The great bulk of infected cows are treated by udder infusion, for which purpose a variety of products are available. Penicillin is used in perhaps the greatest volume. However, other antibiotics, such as dihydrostreptomycin, streptomycin, the tetracyclines, neomycin, polymyxin, and bacitracin, as well as the sulfonamides, are used for treatment and prophylaxis. Experience has shown that the entire amount of infused antibiotic or sulfonamide is eliminated by regular milking over a period of three days. It appears that failure to observe the warning given in the labeling of mastitis preparations concerning the discarding of milk from treated cows is largely responsible for the antibiotic residues that may be present in the milk supply.

During the years 1954, 1955, and 1956, three surveys were made to determine the antibiotic content of fluid market milk. In these surveys, conducted by the FDA, U. S. Department of Health, Education, and Welfare, a total of 2,274 samples were examined. Every state in the United States was included in these investigations. An average of 6.9% of the samples examined contained penicillin in concentrations varying from 0.003 to 0.550 units per milliliter. Other dairy products tested, including powdered milk, evaporated milk, ice cream, butter, cheese, shell eggs, and broken eggs, were found to be free from antibiotic residues.

Recent Advances in Antibiotic Problem

About one year ago a medical advisory panel accepted the invitation of the Commissioner of the FDA to consider the public health problems involved by the presence of antibiotics in market milk. The members of the advisory panel were Drs. Wesley W. Spink, chairman, University of Minnesota; Harry F. Dowling, University of Illinois; Samuel M. Feinberg, Northwestern University; Chester S. Keefer, Evans Memorial Hospital, Boston; Perrin H. Long, State University of New York; Walsh McDermott, Cornell University Medical College; Robert Popper, Veterans Administration Hospital, Memphis, Tenn.; and Bernard B. Siegel, Jewish Hospital of Brooklyn. After an all-day session, during which the problems involved were discussed thoroughly, it was apparent that our main health problem was concerned with penicillin, even though the other antibiotics used in mastitis preparations were found in approximately 1% of the samples examined. It was the consensus of the panel that these antibiotics—the tetracyclines, streptomycin, dihydrostreptomycin, bacitracin, polymxin, and neomycin, which may be found in mastitis preparations, did not at that time pose a public health problem.

It was agreed that penicillin is a very active, antigenic substance and, even in the low concentrations found in milk, might well cause reactions in highly sensitive individuals. It was apparent that the physician should be most concerned in his practice with the latter persons who constitute something less than 10% of the population. It seemed certain that in these individuals reactions could occur. Such reactions could vary in intensity from mild transient ones to possibly serious ones, the serious reactions occurring in those individuals exquisitely sensitive to penicillin. Because scientific proof is essential, it was the consensus of the panel that further studies were necessary with highly sensitive human volunteers to determine whether the ingestion of milk containing those concentrations of penicillin now found in some market milk would cause allergic manifestations.

Recently, the FDA has taken three steps to alleviate the public health problem involved: 1. Through cooperation with the U. S. Department of Agriculture, an intensive program has been initiated to educate the farmer concerning the importance of discarding, or using for purposes other than human consumption, milk from cows treated for mastitis with antibiotic drugs for a period of three days following the last treatment. In addition, the National Milk Producers Federation, which includes some 500,000 farmers, is assisting in this educational program through their state agents. 2. On Jan. 23, 1957, a notice was published in the *Federal Register* concerning the warning statement that is required in the labeling of antibiotic drugs intended for intramammary infusion. It was proposed that for greater conspicuousness this warning be placed on the immediate container of the drug rather than in the literature accompanying it. This is now required. 3. On Feb. 9, 1957, a "Notice of Proposed Rule Making" was published in the *Federal Register,* limiting the penicillin content of mastitis preparations to 100,000 units per dose. This became effective on Aug. 12, 1957.

In the fall of 1958 and the winter of 1959, a fourth nationwide survey of milk was conducted by the FDA to determine if the program discussed above had reduced or eliminated antibiotics from our milk supply. A total of 1,170 samples of raw milk was collected from tank trucks after pickup from dairy farmers or directly from individual producers. Each sample was examined for residues of penicillin, streptomycin, the tetracyclines, bacitracin, polymyxin, and neomycin, all of which are used in the treatment of mastitis in dairy animals. Penicillin, as confirmed by the penicillinase identity test, in concentrations of 0.006 to 1.22 units per milliliter, was found in 43 (3.7%) of the samples. One penicillin-positive sample also appeared to contain streptomycin. Twenty-two additional samples appeared to contain one of the tetracyclines, and one other sample contained bacitracin-like activity. However, there are no specific identity tests for small quantities of these drugs and, therefore, their antibacterial activity cannot unequivocally be attributed to these antibiotics. The results of this most recent survey indicate that the program that was initiated after the third survey has caused a significant decrease in the incidence of penicillin-contaminated milk. In fact, this decrease may be even greater than that shown by the figures because of the difference in sampling techniques used in the 1959 survey and in the previous surveys. In the first three surveys, all samples were collected from milk that had been processed by the dairies and had been delivered to the retail trade. We believe that many of the penicillin-positive samples found in the fourth survey would have been negative if they had been collected after having been diluted with antibiotic-free milk at the dairy, which normally would have been the case. However, the program has not solved completely the problem of penicillin-contaminated milk. It is therefore necessary that other approaches be considered as a solution to this public health problem.

Summary

There are 17 to 20 million individuals in the United States who may react to contact with antibiotics. The physician can avoid unfavorable side-reactions in these people by the discriminate use of antibiotics as therapeutic agents. A greater problem for the physician is the introduction of antibiotics in foods, both directly and indirectly. Antibiotics are used in animal feeds, crop sprays, and as food preservatives. The FDA and other agencies have taken steps to alleviate this problem; however, it has not been solved completely.

ANNOUNCEMENT

A monograph of the five papers presented at the symposium on "Nutrition in Pregnancy" in Columbia, Mo., Oct. 11, 1957, is now available. These papers, which were published in THE JOURNAL, include "Nutritional State of the Mother Prior to Conception" by Genevieve Stearns, Ph.D.; "Maternal Nutrition and the Fetus" by Ray Hepner, M.D.; "Production of Congenital Malformations by Dietary Measures (Experiments in Mammals)" by Josef Warkany, M.D.; "Vanderbilt Cooperative Study of Maternal and Infant Nutrition: XII. Effect of Reproductive Cycle on Nutritional Status and Requirements" by William J. McGanity, M.D., F.R.C.S.(C), Edwin B. Bridgforth, A.B., and William J. Darby, M.D., Ph.D.; and "Metabolic and Biochemical Changes in Normal Pregnancy" by Icie G. Macy, Ph.D., Sc.D. The "Nutrition in Pregnancy" monograph may be obtained, free of charge, from the Council office.

COUNCIL ON MEDICAL PHYSICS

Report to the Council

The Council has authorized publication of the following report. The conditions treated and dosages used represent the author's research and experience. They should not be construed as recommendations of the Council, since the final decision as to dosage and use must rest with the individual practitioner who has examined the patient to be treated. Ionizing radiation for ophthalmic conditions should be employed only by those who are experts and are well aware of the dangers of this form of treatment to the patient and to the physician.

RALPH E. DE FOREST, M.D.,
Secretary.

BETA RADIATION SOURCES, USES, AND DANGERS IN TREATMENT OF THE EYE

William F. Hughes, M.D., Chicago

Beta radiation from radium, radon, and radium D-E has been used in the treatment of certain external ocular conditions for about 40 years because of the relatively superficial effects and accurate localization of the radiation. More recently, radioactive strontium (Sr^{90})-yttrium (Y^{90}) applicators have become available as a source of beta particles or electrons for ocular use. The early enthusiastic reports of the efficacy of beta radiation have been tempered by the appearance of certain secondary complications including cataract. Therefore, it becomes more important that the clinician be aware of the sources, rationale, uses, contraindications, dosages, and dangers of beta therapy.

Characteristics of Various Sources of Beta Radiation

Various sources and applicators have differing characteristics in surface output, depth dose, and amount of gamma rays. A comparison of available data[1] on these applicators is given in table 1. The differences in the construction of the applicators, their output, and depth doses are readily apparent. The earlier method of denoting dosages as "gram seconds" or "millicurie minutes" has no meaning unless the individual applicator is standardized, either physically by means of the Failla-type extrapolation (vanishing ion) chamber or biologically on animal and human eyes. Not only are the outputs of different types of applicators with similar amounts

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of radioactive material different, but applicators of similar design and materials may show significant variations.

Surface Output.—In the past, surface output has been denoted physically as so many reb (roentgen equivalents beta) or rep (roentgen equivalents physical) per second, representing an energy absorption by air of 84 ergs per gram of air per second, or an energy absorption by tissue of 93 ergs per gram of tissue per second. More recently, a new unit of dosage has been officially adopted; namely, a rad, indicating an energy absorption of 100 ergs per gram. Accordingly, for Sr^{90}, 1 rad = 1.19 rep (air) or 1.08 rep (tissue). These numerical values should be considered as guides to clinical dosage rather than be accepted as absolute values. Possible variables include the following factors.

TABLE 1.—*Comparison of Various Sources of Beta Radiation*

Characteristic	Radium		Radon		Radium D-E		Sr^{90}-Y^{90}	
Applicator	Krohmer	Iliff	Burnham (glass bulb)	Hughes (glass needles)	Swanberg		Commercial Applicator No. 1	Commercial Applicator No. 2
Quantity of radioactive material	25 mg.	50 mg.	50-400 mc.	50-300 mc.	10 mg.	20 mg.	25-100 mc.	50 mc.
Size of active surface, mm.	6-8	6x12	4-5	5x7	6.8	6.8	5-7.8	8.7
Inherent filtration	0.1 mm. thickness of magnesium	0.1 mm. thickness of monel	0.1 mm. thickness of glass (approx.)	0.1 thickness of glass (approx.)	0.05 mm. thickness of aluminum or 0.1 mm. thickness of magnesium	0.5 mm. thickness of aluminum or 0.01 mm. thickness of magnesium	0.05 mm. thickness of stainless steel and 0.25 mm. thickness of aluminum	0.1 mm. thickness of stainless steel
Surface output	37 rad.*/sec.	†	0.14-0.5 rad./sec./mc. ave.=0.4 rad./sec./mc.	2-3 rad / sec./mc. (est.)‡	3 rad./sec.	4.4 rad./sec.	approx. 25 rad./sec.-81 rad./sec.	approx. 50 rad./sec.
Part of radiation reaching tissue at depth of:								
1 mm., %	†	17	20-50	†	10	†	41-55	55
2 mm., %	†	8	6-25	†	1	†	19-25	33
3 mm., %	†	4	3-10	†	0	†	7-16	18
4 mm., %	†	2	2-5	†	0	†	4-6	8.5
5 mm., %	†	1	0.8-3	†	0	†	1-3	4
Gamma rays	†	>3.5%	approx. 3.5%	†	none	none	none	none

* Rad.=unit of absorbed dose.
† Data not available.
‡ Estimated by effects on tissues in comparison with other applicators which have been standardized by physical methods.

1. Uneven distribution of the radioactive substance on the inner surface of the applicator may produce a greater error with the extrapolation chamber than with depth doses determined by photographic film determinations. Such unevenness can be detected by underexposing a photographic film with the active surface of the applicator.

2. Filtration by the radioactive material itself (especially radium or radium D-E) or by the window of the applicator can (*a*) increase the depth dose by filtering out beta particles of less energy, although the rad surface output as measured by the extrapolation chamber may be the same, or (*b*) produce more scatter, affecting the extrapolation chamber more than the film method.

3. The surface output is calculated by extrapolation to zero volume of the ionization chamber, successive readings having been taken of the amount of ionization per unit volume produced by the applicator in progressively smaller quantities of air. Estimation of the ionization in "zero volume" is made from the slope of the curve as volume in the ionization chamber is reduced. Unfortunately, the slope of this curve is constantly changing, and the extrapolated estimate of surface output can be as much as 10% in error.

4. Changes in technique of the extrapolation chamber measurements have been made in the past in an effort to approach an absolute value. This has led to confusion in the clinical use of the strontium applicator based on previously established dosages. Recently, this difficulty has not been experienced in restandardization of the applicators.

5. Leakage of radioactive material can occur, resulting not only in loss of potency of the applicator but also in radiational hazard in the environment. This can be tested for by "wipe tests" such as those in which the surface of the applicator is wiped seven times on filter paper, which is then tested for radioactivity with a Geiger tube. The Geiger tube should have a window thickness resulting in a weight of less than 2 mg. per square centimeter. Under regulations of the Atomic Energy Commission, one would not be authorized to purchase a Sr^{90} applicator unless adequate facilities existed for carrying out a wipe test. Sr^{90} applicators should be rechecked and restandardized, especially if there has been a positive wipe test. The user should also be warned to keep his hands from the front of the applicator when wiping the surface. It is also a good idea to attach to the storage box a decay curve showing the activity over one half-life, e. g., 25 years for the Sr^{90} applicator.

How can an ophthalmologist or radiologist be certain of the clinical effect to be expected from a certain applicator? Evenness of layering of the radioactive material can be checked with x-ray film. The surface output and depth doses can be determined on each applicator by the company which issues the applicator. Biological standardization is the only means at present of determining the output of applicators with unusual shapes and is a valuable check on the physical methods of measurement. This can be performed on the rabbit cornea. The applicator is placed in steady contact with the rabbit cornea, preferably using six corneas for each dose of 15,000, 20,000, 25,000, and 30,000 rad. The minimal dose that produces a faint corneal opacity which does not clear for several weeks has been termed the "Minimal Inflammatory Dose" or "MID" by Wilson. For the Sr^{90} applicator, this is approximately 21,000 rad ± 10%.

Depth Doses.—Surface output does not necessarily indicate clinical effectiveness or possible dangers of cataract formation. Because true absorption or ionization in tissue cannot be measured directly, a measurement in the ionization chamber can be made after the beta particles have passed through varying thicknesses of tissue-equivalent material, for example, polystyrene, lucite, or water. Ideally, selection of beta sources with beta particles of different energies and depth doses might be made with regard to the depth of the lesion to be treated. For example, prevention of the superficial vascularization of a recurrent pterygium would require only surface irradiation, whereas deeper irradiation would be indicated for tumors or deep corneal vascularization. Knowledge of depth doses is also important in relation to possible formation of cataract. In applying contact therapy to the corneal limbus, the sensitive equatorial cells of the lens are only 3 mm. away, whereas the anterior surface of the lens is usually about 4 mm. distant from the apex of the cornea. With this information, an estimate can be made of the amount of radiation reaching the lens. The tolerance of the lens for irradiation will be discussed under dangers of beta radiation.

TABLE 2.—*Relative Proportion in Tissues of Beta and Gamma Radiation from Radon*

Tissue Depth, Mm.	Beta Radiation, %	Gamma Radiation, %
0 (Surface)	96.5	3.5
1	88.0	12.0
2	78.5	21.5
3	67.6	32.4
4	55.5	44.5
5	43.0	57.0

Gamma Rays.—Radium and radon applicators, unlike radium D-E and Sr^{90} applicators, emit gamma radiation in addition to beta radiation. The relative proportion of beta to gamma radiation from radon at various tissue levels is found in table 2. Because of the relatively small amount of gamma radiation in comparison to the beta particles which emerge from radon, a therapeutic dose of beta radiation can be applied to superficial tissue without undue gamma ray absorption in the deeper structures of the eye. The percentage of gamma rays is somewhat greater in radium than in radon applicators because of the absorption of beta particles by the radium mass itself. This results in a loss of clinical potency of beta radiation from the radium applicator, which might be roughly estimated as 15% per unit area for the Iliff applicator. Accordingly, with the radium applicator, a longer exposure time, with consequently more gamma radiation, is necessary to obtain the desired dosage of beta radiation than is the case when radon is used. From a practical standpoint, gamma radiation from beta applicators creates some hazard for the therapist. These applicators should be stored in a lead container with walls, top, and bottom at least one inch in thickness. The lids should be held open by a speculum, by the patient, or by another person not connected with radiation therapy. The maximum permissible dose for the therapist should follow the recommendations of the National Committee on Radiation Protection.[2]

Characteristics of Applicators.—In an effort to encourage more uniformity of beta radiation applicators, certain information about the characteristics of each applicator is desirable, as follows: (1) the quality of radioactive emanations, including the ratio of beta to gamma rays and energy of the beta particles (maximum Mev, average Mev, and depth doses); (2) certification by the National Bureau of Standards or by a qualified laboratory of the quantitative output of each individual applicator in rad surface output; and (3) experimental and clinical trials to corroborate the output.

With the need for the information just outlined, a few comments on the deficiencies of the various applicators are in order. In the radium applicators, the surface output in rad per second has not been standardized physically, the depth doses have not been determined, and biological determination of the MID has not been published.

A specimen of an early model radium D-E applicator was tested for surface output and depth dose, but each individual applicator has not been standardized. Wilson [1d] found that the radium D-E applicator required approximately two and one-half times the dose in gram seconds of radon to produce similar clinical effects in both rabbit and human eyes. This lower clinical potency of the radium D-E applicator is probably the result of the self-absorption of the relatively soft beta particles by the radium D mass itself, plus the smaller depth doses of the less energetic beta particles. Doubling the quantity of radium D in the applicator does not double the output but instead increases the effectiveness by approximately 50%. Because of the relatively low output of the 10-mc. radium D-E applicator, either prolonged treatment times up to 16 minutes are required to eliminate such a condition as superficial corneal vascularization, or repeated exposures within relatively short periods of time (e. g., every week) are required to obtain adequate cumulative effects. These considerations are of some practical importance clinically, because prolonged treatment times increase the difficulty of accurate localization of the radiation and increase the amount of trauma. The relatively low depth dose makes it difficult to obtain adequate dosage in the treatment of such conditions as deep corneal vascularization without excessive damage to the superficial tissues.

The radon applicators have the inherent disadvantage of deterioration (half-life, 3.825 days), and it is practically impossible to standardize each applicator after reloading. Krohmer[1a] measured several radon applicators physically and found that the surface output varied as much as 63%. Also, the construction and shape of some radon applicators have prevented measurement of the output by ionization chambers.

The characteristics just outlined for each applicator are available for Sr^{90} applicators. This assumes that the present physical methods of calibrating the applicators by the issuing companies remain the same, and that one rad surface output today will correspond to one rad surface output on which the clinical dosages have been determined previously.

Use of Beta Radiation

The general uses for beta radiation are the same as for any other type of radiation such as x-ray. The effects of irradiation are destructive, and there must be a differential sensitivity between the pathological cells to be destroyed and the normal cells of the adjacent tissue. The relative sensitivity of cells to radiation has been determined previously by Desjardins[3] and others in the following order of decreasing sensitivity: lymphoid cells, polymorphonuclear cells, eosinophils, epithelium (conjunctiva, cornea, lens, and ciliary), endothelium (vessels, cornea), connective tissue including the cells of the corneal stroma, muscle, bone, and nerve which includes the neural elements of the retina. Among other factors which increase the sensitivity of cells are undifferentiation, immaturity, premitotic stage, active metabolism, and a large blood supply. Very small doses of irradiation are stated to affect favorably infectious processes, although larger doses are detrimental.

Method of Administration.—The method of administration of beta radiation is as follows. Slit-lamp examination is performed to determine the exact area for treatment. Topical anesthesia is then applied and the applicator placed in contact with the lesion. Unless the total dose is purposely fractionated or a severe condition warrants more frequent treatments, at least two to three months should be allowed between treatments in order to observe the maximal beneficial effects of the previous treatment and thus utilize the smallest effective dose. However, as shown in other sections of this paper, determination of maximal deleterious effects requires a greater time interval. When the Sr^{90} applicator is employed, probably not more than 4,000 rad per area of treatment should be used, unless the possibility of later lens opacities is considered to be a legitimate risk. A dose of 1,000 rad may be sufficient for highly sensitive lesions.

Conditions Treated.—Because of the uncertainties in dosage and the development of late complications, beta radiation should be reserved for use in those conditions in which it is superior to other methods of treatment or in which other methods have failed. This conservatism has reduced the number of conditions in which beta radiation is recommended. It is not the purpose of this communication to give in detail the dosages and results of beta radiation therapy in many conditions. Recently, a study has been made of 694 eyes previously treated with radon (60% of cases) or a Sr^{90} applicator.[4] In about half of the cases patients were followed up for over five years, and in some of the early cases patients treated with radon were followed for as long as nine years. In general, the results of treatment and the complications were essentially the same, whether a Sr^{90} applicator or a radon applicator[1b] had been used. As an approximation of dosages of equal clinical effectiveness, one gram second of beta-radon was roughly equivalent to 2,000 rad with the Sr^{90} applicator. The currently recommended dosages in rad given subsequently apply to the Sr^{90} applicator.

Favorable Results of Treatment with Beta Radiation

Corneal Vascularization.—The undesirability of corneal vascularization and the relatively great sensitivity of the endothelium of blood vessels to radiation have led to the use of beta radiation in preventing or eliminating corneal vascularization. In general, superficial vessels are more sensitive to treatment, probably because they receive a larger dose of radiation. Small, actively growing capillaries on the surface are very sensitive, thereby providing an effective means of preventing recurrences of pterygiums after operation. Large trunk vessels, especially when deep, require such large doses of radiation that the long-term results are usually disappointing. The most gratifying results both subjectively and objectively were obtained in cases of rosacea keratitis, which were resistant to local corticosteroid therapy, in which only 2 out of 42 patients remained unimproved and none became worse after radiotherapy. The effective dose in any one quadrant of the cornea necessary to eliminate the corneal vascularization of rosacea keratitis approached the minimal dose which might produce small peripheral opacities in the lens a few years later, namely, 6,000 rad. The primary treatment of pterygiums or their recurrences by beta radiation required unduly large doses to eliminate the well-established vessels. However, beta radiation given within one to two weeks after operation appeared effective, with only 1 case of 42 recurrent cases of pterygiums recurring after this combined treatment; none of 81 cases of primary pterygiums treated with surgery and prophylactic beta radiation developed any recurrence. Although a larger series with proper controls is required for final evaluation, the present management for very vascular or recurrent pterygiums consists of operation, followed one week later with 1,000 to 2,000 rad of beta radiation, repeated once one to three weeks later.

Limbal Tumors.—All 22 cases of tumors at the corneoscleral junction responded well to beta radiation, either with or without partial excision, including papillomas, epithelial plaques, Bowen's disease (epidermoid carcinoma in situ of skin), and epitheliomas (11 cases). A dose of 5,000 rad is recommended for premalignant and malignant tumors, and 3,000 rad for papillomas.

Vernal Catarrh and Allergic (Phlyctenular) Keratitis.— Vernal catarrh and allergic conditions of the conjunctiva and cornea are usually alleviated by the local use of corticosteroids such as hydrocortisone or prednisolone. However, certain cases do not respond satisfactorily or have frequent recurrences. This is particularly true of palpebral vernal catarrh, with large pavement-stone vegetations and ropy discharge, and of allergic keratitis of the lower portion of the cornea associated with superficial vascularization. The effects of beta radiation have been helpful in most of these cases. In general, doses of 5,000 rad are given to each area of the vernal catarrh on the upper lids, care being taken not to expose the roots of the lashes. Such doses can be repeated once or twice, if necessary, after several weeks or a few months. For limbal lesions of this type, doses as low as 1,000 to 2,000 rad, perhaps repeated once after a few weeks, may be sufficient to eliminate this allergic type of tissue and superficial vascularization.

Conjunctival Papillomas and Hemangiomas.— These benign tumors are very sensitive to beta radiation and can often be eliminated by doses as low as 2,000 rad.

Trichiasis.—The dosage required for permanent epilation is uncertain, but it can usually be accomplished by 3,000 rad of beta radiation. However, the eyeball should be carefully shielded.

Variable Results of Treatment with Beta Radiation

Good results were obtained in only 30 to 40% of the following types of corneal vascularization: primary vascularizing keratitis, indolent corneal ulcer, chemical burns, effects following corneal transplantation, scars of unknown etiology, trachoma, corneal dystrophy, and keratoconus. Six cases of interstitial keratitis showed no change attributable to the radiation. Although various types of keratitis, episcleritis, and scleritis often showed improvement after treatment with very low doses (500 to 1,000 rad) of beta radiation, it could not be determined whether this was significantly related to the radiotherapy. Although granulation tissue is sensitive to radiation, the results after beta radiation therapy were variable, possibly because the depth dose was insufficient to reach the deeper portions of the granulation tissue usually located within the tarsus of the lid. Therefore, it is inadvisable to use this radiation to treat such granulation tissue. Merriam[5] reported that precancerous melanosis of the conjunctiva responds satisfactorily to 3,000 to 5,000 rad of beta radiation.

Contraindications for Use

Beta radiation should not be used for several conditions because of lack of effect, better treatment available, or undesirable complications. These include tumors of the lid margin, nevi of the conjunctiva, pinguecula, primary treatment of pterygiums without immediately preceding surgery, pemphigus, corneal scars without vascularization, Fuchs' endothelial-epithelial dystrophy, epithelial downgrowths into the anterior chamber, acute chemical burns, and inflammatory lesions, requiring large doses.

Complications of Beta Radiation

Cataracts.—Any opacity in the lens, with or without reduction in vision, is termed a cataract. With this definition, cataracts have been observed in both rabbits and humans after beta radiation from radium, radon, and Sr^{90} applicators.[6] Treatment over the limbus is most likely to produce lens opacities because the sensitive germinative cells at the equator of the lens are only 3 mm. away from the surface of the limbus, and from 4 to 18% of the surface dose from these applicators reaches this area.

In the study referred to previously,[4] no radiation cataracts were observed in any of the 192 patients treated for conditions of the lids. A total of 213 eyes, which had received beta radiation treatment to the globe, were examined to determine the presence or absence of radiational lens opacities. Of these, 45% had definite radiational opacities, and 12% had probable radiational opacities. The earliest cataracts were seen two and one-half years after treatment, larger doses producing opacities somewhat earlier than smaller doses. The smallest dose which produced equatorial vacuoles in the lens was 4 gram seconds when the radon applicator was used and 5,000 rad when the Sr^{90} applicator was used. On the other hand, other eyes showed no evidence of cataracts for as long as eight years after exposure to 12 gram seconds of radon or three years after exposure to 7,000 rad of strontium^{90}. Peripheral radiational vacuoles in the lens usually assumed a wedge-shaped configuration and, with larger doses of radiation, migrated posteriorly. Of the cases observed both in 1953 and 1957, 79% showed progression of the opacities, 11% no progression, and 9% showed actual regression. Of 121 eyes with definite or probable radiational opacities, 19 previously treated with radon and 7 previously treated with Sr^{90} had opacities which reached the posterior pole of lens where they might have interfered with vision. Two beta radiation cataracts were extracted, and three additional cataracts were extracted from eyes which had received both x-ray and beta radiation.

Other Complications.—A year or more after administration of doses as low as 7,000 rad to the conjunctiva, telangiectases developed in and around the area of radiation. In one-third of these cases, these postradiational vessels created a real cosmetic blemish, especially when located within the palpebral fissure. Interference with wound healing was noted in approximately half of the 17 corneal transplantations and 10 cataract extractions performed on eyes which had been treated with beta radiation from six months to nine years prior to surgery. This confirms the previous experimental results in rabbits.[7] Since radiation is primarily destructive, the therapist must be careful to avoid accentuation of necrosis and ulceration already present. This is particularly true of acute chemical burns, corneal ulcers, and inflammatory processes.

Summary

Beta-radiation ophthalmic applicators, particularly the radioactive strontium (Sr^{90})-yttrium (Y^{90}) applicator, provide a ready source of radiotherapy for superficial lesions of the eyes. The general indications for beta radiation of the eye are the same as those for other forms of radiation such as x-ray. Because the therapeutic dosage and the dosage which might result in later complications are fairly close, exact knowledge must be obtained concerning the output of the applicator in rad per second, the depth dose, biological standardization, and the differential sensitivity of the tissues to be destroyed compared with the normal ocular tissues. This is particularly important when radiation is given over the region of the limbus which is only 3 mm. away from the sensitive equatorial region of the lens. Minimal cataractogenic doses appear, at this time, to be approximately 5,000 rad at the applicator surface with the Sr^{90} applicator when applied over the limbus. Minimal lens opacities in the periphery do not necessarily progress or affect vision, and certain serious ocular conditions requiring beta radiation warrant the necessary risk of producing a cataract later. In general, beta radiation should be reserved for use in those ocular conditions in which it is superior to other methods of treatment or in which other methods have failed.

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ACCIDENTS IN CHILDHOOD.—The death rates from accidents actually declined 42 per cent from 1928 to 1957. This decline is primarily due to improvement in the care of the victim and not the result of a decrease in the rate of accidental injury. During the same period, however, mortality from most other causes in childhood declined even more dramatically, leaving accidents as the most common serious health problem of childhood today. Home accidents account for 38 per cent of all accidental deaths in children under fifteen years of age, and in the age group under five, 58 percent of accidental deaths occur in or about the home.—R. J. Haggerty, M.D., Home Accidents in Childhood, *The New England Journal of Medicine,* June 25, 1959.

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PROBLEMS OF IMPAIRED SPEECH AND LANGUAGE

GUEST EDITORIAL

Wendell Johnson, Ph.D.

THE process of symbolization is the most distinctively human of man's bodily functions. The clinically recognized impairments of the symbolization process are primarily those of spoken language. Disorders of spoken language involve impaired phonation, speech sound articulation, fluency and rate, or symbolic representation, singly or in combination, associated or not with significant organic or physiological complications or emotional disturbance.

The clinically significant organic or physiological conditions most often associated with speech problems are those related to hearing loss, cleft palate, laryngectomy, cerebral palsy or other types of neuromuscular impairment, brain damage including cerebrovascular accident with attendant aphasia and dysarthria, and retarded or limited development affecting language and speech. Associated emotional reactions are rather more likely to be effects than causes of the speech disorder, and are, in any event, interactive with it.

The magnitude of the problem is suggested in part by current estimates of incidence. I recently had occasion to appraise relevant aspects of the situation for the United States Office of Education and concluded that probably 4% of all children enrolled in the public and private elementary and secondary schools of the United States have socially and educationally significant speech problems.[1] This amounts to a total of 1,600,000, assuming a national public and private school enrollment of 40 million. About 1 million of these children present faults of articulation, such as lisping, not associated with organic pathology. About 280,000 school children stutter, 200,000 have impaired speech associated with hearing loss, 40,000 have voice problems, and about 20,000 present each of the following faults: fluency and rate problems, retarded speech development, speech difficulties related to cleft palate and lip, and problems of speech and voice associated with cerebral palsy and other types of disturbed neuromuscular functioning.

Incidence data for adults are limited. There are, certainly, relatively more cases of functional misarticulation among children and more cases of aphasia and impaired speech and voice associated with laryngectomy and vocal cord pathology among adults. Stuttering affects from 6 to 8 per thousand children and college-age adults, but the incidence for more advanced age levels has not been well determined. Decreased auditory acuity and other effects of aging tend to be reflected in modified speech and language, with varying degrees of personal and social significance.

Present knowledge indicates that, by conservative estimate, there are probably 2,500,000 children and adults in the United States with speech, voice, and language impairments of relatively severe grade.[2]

The problems presented by these 2,500,000 persons are both medical and nonmedical, and they are most constructively managed through flexible patterns of multidisciplinary cooperation, varying with the needs of specific speakers. The medical specialists most often concerned with conditions functionally related to speech, voice, and language disorders are the otolaryngologists, oral surgeons, neurologists, neurosurgeons, orthopedic surgeons, psychiatrists, pediatricians, and general practitioners.

The nonmedical profession that has developed in response to the growing demand for educational and remedial services in this field is that of speech pathology and audiology, representing the speech and hearing sides of the coin of impaired communication.[3] This profession functions through the American Speech and Hearing Association (1001 Connecticut Ave. N. W., Washington 6, D. C.), which administers clinical certification for its members at basic and advanced levels in speech and hearing, respectively, publishes the *Journal of Speech and Hearing Disorders* and the *Journal of Speech and Hearing Research,* and seeks to improve the research and professional training programs and the educational and clinical services within its sphere of responsibility. Two-thirds of its roughly 5,000 members hold graduate degrees, and some members are physicians.

As a profession, speech pathology and audiology synthesizes the resources of several scholarly and scientific fields, particularly phonetics, semantics, psychology, psychoacoustics, genetics, anatomy, physiology, and neurology, as well as education, sociology, and cultural anthropology. Within the resultant interdisciplinary framework a growing body of research data, theory, and clinical technique has been accumulated. The number of uni-

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From the Department of Speech Pathology and Audiology, State University of Iowa, Iowa City.

versities with departments of speech pathology and audiology and graduate programs in the field is gradually increasing. An estimated 1,000 to 1,200 graduates at all degree levels are being trained annually and an increasing refinement of the profession's standards of training parallels its growth. Other professions which contribute substantially to the effectiveness of services for persons with speech impairment are dentistry, particularly orthodontia and prosthodontia, education, and clinical psychology.

Speech correctionists do their work for the most part in two general settings: (*a*) the schools and (*b*) university and community speech and hearing clinics, hospitals, hospital-schools, rehabilitation centers, and institutions for the handicapped or retarded. So far as sheer number of cases is concerned, most speech correction is done in the public schools, primarily in the early grades. Most public school speech correction cases are those involving speech sound misarticulation without organic or severe emotional complications. Although school personnel commonly devote time to persons with organic speech problems and to those with complex emotional involvements, the services rendered tend to be demanding and extremely time-consuming. Moreover, they must be coordinated with essential medical and surgical measures, and as a consequence these more complex speech problems are generally dealt with wholly or in part in speech clinics outside the school.[4] Many universities conduct intensive summer speech clinics for school-age children.

Since speech correction is severely demanding of time and attention to detail,[5] and because of the nonmedical character of the required specialized training, it is the exceptional physician who is disposed to prepare himself by formal training to assume responsibility for speech correction, per se. Meanwhile, most physicians have a constant opportunity and ever-recurring obligation to consult with professional workers in speech pathology or to secure for their patients needed speech correction services. This is particularly true in patients requiring surgery that clearly or possibly will affect the speech function, as in cleft palate repair and laryngectomy. It is true as well in the development of an optimal rehabilitation program in any case of neuromuscular dysfunctioning involving the speech mechanism. Adequate treatment and care in cases of cerebrovascular accident necessarily include appropriate speech and language appraisal and indicated retraining procedures. Maximally effective treatment for patients with impaired hearing involves, as a matter of course, not only essential audiological measures with respect to hearing aids and auditory training but instruction and counseling designed to restore or preserve clear and well-modulated speech.

Pediatricians and general practitioners have frequent need to give counsel in response to parental concern over childhood speech—especially when such concern is not justified and is most likely, therefore, to have harmful effects. Little doubt remains that stuttering, for example, originates primarily in the disturbing perceptions and judgments of the listening parent responding with ill-informed preconceptions to the child's normally hesitant early attempts to negotiate the intricate neuromuscular and psychosocial complexities of spoken language.[5] We know now that the problem we call stuttering is not to be confused with the matter (it is seldom a problem) of speech nonfluency, per se.

Considerable research to date provides no appreciable support for the hypothesis that stuttering is characteristically associated with or symptomatic of severe emotional disturbance or neurosis in a clinically significant sense.[7] The counseling and retraining procedures needed by adolescent and adult stutterers, as well as by most persons with other types of impaired speech, appear to be, in their own way, of a piece with those required by the handicapped and mistutored rather than the neurotic or emotionally unstable.

The significance of the process of symbolization in relation to health and disease awaits the definitive scientific appraisal that its distinctively human character urgently warrants. Its role in the iatrogenic[8] and semantogenic[9] disorders would appear to be basic. It seems likely that it provides the major mechanism for psychosomatic reactions and for the patient's mode of adjustment to illness of whatever sort—and to wellness. The overriding consideration is that symbolization is a bodily process, mediated by the nervous system, and that it interacts necessarily with other bodily functions. There is little to be said for disregarding its gross disorders; there is much to recommend sophisticated attention to its seemingly minor but innumerable miscarriages.

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ORGANIZATION SECTION

STATEMENT TO SUBCOMMITTEE ON HEALTH AND SAFETY

July 6, 1959

Hon. Kenneth A. Roberts, Chairman
Subcommittee on Health and Safety
Committee on Interstate and Foreign Commerce
House of Representatives
Washington 25, D. C.

Dear Congressman Roberts:

This will acknowledge with thanks the notices dated June 18, 1959, addressed to me as Executive Vice President of the American Medical Association, and to Dr. Fletcher D. Woodward, the Chairman of our Committee on Medical Aspects of Automobile Injuries and Deaths. With your permission the Association would like to submit this statement for inclusion in the printed record of the hearings on the measures outlined in the notice of June 18.

Inasmuch as the American Medical Association has not considered or taken a position on most of the specific bills under consideration by your Committee, our statement will be general in nature. It will, however, I believe, outline the extent of our interest in this field and underscore our conviction that regulatory action at an early date is imperative.

The American Medical Association has been concerned with the problem of automobile injuries and deaths for many years. Actions of our House of Delegates on this subject are numerous and date back as far as 1929. In 1948, our House passed the following Resolution:

> WHEREAS, The American Medical Association has in the past cooperated with the National Safety Council in its efforts to reduce the incidence of deaths and injuries from accidental causes; and
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> WHEREAS, The studies that have been made by the Bureau of Medical Economic Research of the American Medical Association have established the fact that fatal accidents cut off more years from the working lifetime of the American people than any one natural cause of death, and
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> WHEREAS, In the recent report made to the President by the administrator of the Federal Security Agency, it was stated that 40,000 deaths annually from accidents were preventable; therefore be it
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> *Resolved,* That the Board of Trustees be instructed to cooperate in every possible way with the National Safety Council and with every other agency, both public and private, concerned with accident prevention, to the end that research in accident prevention be further stimulated; that this excessive drain on hospital and medical facilities be lessened, and that the appalling loss of working years be reduced.

For more than 30 years our Association has had Committees actively working on the various aspects of the automobile accident problem. The present Committee, known as the Committee on Medical Aspects of Automobile Injuries and Deaths, was appointed by our Board of Trustees in 1955. Its members are chosen from physicians who by their interest and work are considered to be well qualified in this field.

We believe most people will agree that those who are called upon night and day to pronounce dead those persons killed on our highways, and who mend the broken bodies of those who are injured, can well be classified as interested and qualified in their efforts to prevent such carnage. Within the lifetime of most of us, we have seen substantial gains by the medical and allied health professions in the conquest of disease and disability. Many of the diseases that were commonplace early in this century have been conquered or brought under effective control. Many diseases that were once widespread are now a rarity. However, accidental injuries and disabilities due to automobile accidents have become the number one public health problem of our time. We believe it is important, therefore, that the medical profession continue to increase its interest in the automobile accident problem until effective improvement is a reality.

As the result of our studies, we are convinced that if speed, recklessness and drunken driving are controlled, and if improvements in automobile engineering are provided to protect those involved in collisions, then the present appalling toll of injuries can be substantially reduced. We are further convinced that enough facts are at hand to accomplish this purpose.

One of our most important objectives has been to provide the practicing physician with technical medical information which will enable him to advise and inform his patients relative to driving limitations that may be involved because of the effects of drugs or alcohol or the existence of physiological, pathological or emotional conditions.

We realize that a certain percentage of accidents are undoubtedly caused directly or indirectly by medical conditions, drugs, and other related physical factors. In an effort to identify these problems and to develop workable solutions, we sponsored a symposium on Medical Aspects of Automobile Injuries and Deaths at the Association's Annual Meeting in June, 1956, in Chicago, and in June, 1958, in San Francisco. Papers presented at these meetings were published in THE JOURNAL of the American Medical Association on January 26, 1957, and April 4, 1959. Reprints are attached for you and for the members of your Committee.

Our next objective was to prepare a comprehensive book to serve as a guide to physicians in determining fitness to drive as related to the medical background of the individual. This book, a copy of which is attached, represents a compilation of medical data and the opinions of nationally recognized authorities in the various special fields of medical practice. With this information available, it should be possible for the individual physician to make a significant contribution to the welfare of his personal patients and the public at large.

Closely related to the need for factual information to aid the physician is the need to inform the driving public, through use of proper media, of the medical conditions which may affect their driving proficiency. We believe that many individuals would voluntarily discontinue or diminish radically their driving if they understood the dangerous possibilities involved in certain physical disorders and the potential effects of certain medications. In other words, we believe the technical information furnished the physician should be supplemented with a pamphlet written at the popular level and covering the more commonly encountered medical situations. In this way the patient can have the advantage of written information which will serve to instruct him as to whether he should or should not drive; and, if so, under what safeguards. Such a pamphlet, entitled "Are You Fit to Drive?" has been prepared by our Committee on Medical Aspects of Automobile Injuries and Deaths, in cooperation with the Center for Safety Education of New York University.

There is little doubt that a great deal of attention must be given to the very serious question of who shall be permitted to drive an automobile and who shall be denied that privilege. We emphasize that driving should be a privilege rather than a right. Therefore, our third objective is to develop better medical standards for driver licensing, including preparation of a guide for license examiners and assistance to state agencies concerned with licensing. This will be based on the information compiled in the medical criteria mentioned earlier and will constitute our recommendations for state licensing agencies. We recommend that each state medical society have a committee on traffic safety, with objectives such as those outlined on the attached green sheet. Such committees would be in a position to advise and assist state driver licensing bodies in the improvement of medical standards for licensing.

Another objective is to study and report on the design features of automobiles. Improvement of the design and safety equipment of automobiles promises the greatest possibility for rapid reduction in the automobile injury and death toll. If it is estimated that the average life of an automobile is ten years, it is apparent that a very considerable reduction in the severity of injuries and a marked reduction in fatalities could be accomplished in that time if more attention were devoted to providing safety rather than to increased horsepower, streamlining, color, and chrome.

The engineers and designers of the automobile—a relative handful of men in the industry—virtually control the destinies of the American public on the highways. They are the men who decide which elements of safety design will be put into or left out of next year's new automobile.

There is presently available an ample body of research data which clearly indicates the definite values of certain safety features of automobile design, construction and equipment. Yet, these safety features, if available at all, are all too often offered as optional equipment at extra cost. The automobile industry can make a great contribution toward solution of this problem by consulting with physicians, anthropologists, psychologists, related biological scientists, and other scientific professions, and by giving realistic consideration to the wide range of physical characteristics of automobile drivers and riders and what happens to them in a collision.

In the past the automobile industry has made many important contributions to safety. However, in recent years, safety has generally been ignored in favor of other developments. The following suggestions have been repeatedly advanced by physicians, researchers, and safety engineers with but little success:

1. Anchorage for seat belts should be standard equipment. The public also needs education in the value of seat belts. The only evidence so far presented against seat belts is in the number of deaths in sports cars during roll-overs. This is not an argument against seat belts but against the design of such cars which do not provide roll-over bars. It should be quite simple to incorporate such a bar in the windshield and a second one back of the seat.
2. Crash padding of the dash, roof, and other areas should be provided.
3. An improved steering wheel and recessed post; perhaps a collapsible assembly.
4. Safety door locks should be standard in all cars.
5. Removal of dangerous knobs, buttons, sharp edges, and other gadgets.
6. Seats should be securely anchored to the floor of the car and should be locked into position. They should also be high enough in the center to protect the neck in a rear-end impact and prevent neck-snap injury (also called whiplash).

7. Eliminate the deck behind the rear seat as a storage place for flying missiles or provide it with an effective retaining rail or construct it as a recessed pocket.
8. Eliminate sharp, pointed hood ornaments. These fill no functional need and are potentially lethal to pedestrians.
9. Eliminate other hazardous exterior design features such as sharp, pointed bumper ornaments.

In addition, we feel that the automobile industry should make an open-minded examination of other suggestions and adopt them where feasible. For example:

1. Shock-absorbing bumpers: if one drives his car into a brick wall at one mile per hour, he will be astounded at the shock transmitted by such an impact. One person testifying last year intimated that to absorb the energy at 20 miles per hour in a 4,000-pound car, such a bumper would have to be 16 feet long.
2. Polarized headlight lenses and an oppositely polarized windshield spot. They would prevent glare at night and thereby prevent many pedestrian accidents and deaths.
3. Consideration should be given to the design of windshield and rear windows to meet standards based on optical principles.
4. Provide protective side-swipe bumpers along the sides.
5. Provide warning reflectors on the sides.
6. Remove tail lights from the realm of the artistic designer.
7. Provide a positive separation of turn signal lights from other lights.
8. Eliminate the glare-reflecting surfaces on the interior.
9. Provide accurate speedometers. Why do we have speedometer dials indicating up to 120 miles per hour? Why not an audible warning device to denote when safe speed has been passed?
10. Construct drivers' seats with better regard for the posture and visibility of persons of various heights.
11. Make chrome, clocks, radiator ornaments and other expensive gadgets optional equipment and install safety equipment as standard equipment.

The following Resolution adopted by the House of Delegates of the American Medical Association at its meeting in Boston on December 1, 1955, is evidence of the interest in this subject by the entire medical profession and the conviction that something constructive can and should be done toward the prevention of injuries:

> Whereas, Traffic accidents in the United States claim 38,000 lives and 1,250,000 injured each year, with a probable 45% increase in vehicle mileage in the next ten years; and
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> Whereas, This death and accident toll could be materially reduced through improvement in automotive safety design and construction; and
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> Whereas, All other modes of public transportation except automobile are already safeguarded by Federal safety standards; therefore be it
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> *Resolved,* That the American Medical Association, through its House of Delegates, strongly urges the President of the United States to request legislation from Congress authorizing the appointment of a national body to approve and regulate safety standards of automobile construction.

On January 9, 1956, Dr. George F. Lull, who was at that time Secretary and General Manager of the Association, addressed a letter to President Eisenhower in which he directed attention to the Resolution.

Another objective of the Association is to promote the extension of emergency first aid training to as many citizens as possible. This training will be of value not only in connection with the reduction of the severity of automobile crash injuries, but also in connection with civil defense needs as well. We feel it is also desirable, therefore, that all automobiles be equipped with first aid kits.

Related to first aid is another objective—to assist in the promulgation and to promote the use of standards for organized emergency services in local communities, including training of rescue squads and standardized equipment for rescue vehicles. This is a future activity in which we will work through state and county medical societies. An example of one problem in this area is the need for better selection, education and control of drivers of emergency vehicles.

As citizens and physicians, we recognize the importance of driving courses for all high school students. Similar courses should be provided for the public and the curriculum should meet certain basic educational requirements. We sincerely hope the day will soon come when such certificates will be required of all prospective drivers as well as for repeat traffic law violators.

Since speed and driving under the influence of alcohol and their related offenses are intimately associated, we feel that strict legislation in this field should be provided. The public needs to be aroused to the point whereby the legislators will provide these laws and the traffic courts will administer them without fear and with complete impartiality.

Because of the indefatigable work of many safety organizations over the years, the incidence of death has been greatly reduced in spite of the tremendous increase in the number of vehicles and number of miles traveled. In spite of this apparent success as to the incidence rate, the total number of deaths and injuries is increasing each year. Unless some of the suggestions mentioned above are followed, it seems inevitable that this number will continue to increase despite the splendid work now being done.

Your willingness to permit the American Medical Association to present its views with respect to the legislative proposals under consideration by your Committee is sincerely appreciated.

Sincerely yours,
F. J. L. Blasingame, M.D.
Executive Vice-President

STATEMENT OF DR. GEORGE M. FISTER ON H. R. 10, BEFORE FINANCE COMMITTEE OF SENATE

Mr. Chairman and Members of the Committee:

I am Dr. George M. Fister of Ogden, Utah, where I am engaged in the private practice of medicine. I am a member of the Board of Trustees and the Chairman of the Council on Legislative Activities of the American Medical Association. With me is Dr. Vincent W. Archer of Charlottesville, Virginia, a member of the American Medical Association's House of Delegates and a member of our Committee on Federal Medical Services.

We are here today as representatives of the American Medical Association to express the wholehearted support of the medical profession for H. R. 10, 86th Congress, a bill which, if enacted, would provide a measure of tax equity for the self-employed including physicians in private practice.

I shall not review or attempt to summarize the provisions of the pending bill since I am sure that you are all completely familiar with the measure. I would like to restate very briefly, however, the history of the support of legislation of this type by the American Medical Association.

In 1948 our Board of Trustees was apprised of a movement to encourage the enactment of Federal legislation which would enable self-employed persons, including physicians, to provide for their own retirement benefits through the payment of amounts annually from their taxable income to finance retirement plans. The Board approved this movement, suggesting that there be a reasonable limitation on such retirement benefits. This action was endorsed by our House of Delegates, the governing body of the Association, at its meeting in June, 1948.

In June, 1951, at the annual session of the American Medical Association, three resolutions emphasizing our endorsement of this principle were adopted by the House of Delegates. On numerous occasions since that time the House has reiterated this endorsement and has recommended that each member of the Association give the matter his careful study and active support.

In the 82nd, 83rd, 84th and 85th Congresses, the Association, through its representatives, expressed support of this type of legislation before the Ways and Means Committee of the House of Representatives. A similar expression of support was communicated by letter to that Committee earlier this year. We have also collaborated closely with representatives of the American Bar Association, the original sponsors of this measure, and other national organizations of self-employed taxpayers who would be covered by the provisions of the bill.

It is the belief of the American Medical Association that physicians, dentists, farmers, lawyers, architects, veterinarians, merchants, and the many others who comprise the nation's self-employed have long been neglected in Federal tax legislation relating to pensions. Under existing law, corporations are entitled to set aside tax-free money to purchase pensions and annuities for their employees, and millions of employees are benefiting from that arrangement. With high taxes and inflated living costs, it is difficult for the self-employed person to set aside adequate funds for retirement without a tax deferment similar to that available to corporate employees. The purpose of this bill is to eliminate this discrimination and inequity. By extending the tax deferment privilege to the country's eleven million self-employed, this legislation will give them an opportunity during their best earning years to save for their old age.

Unless something is done to make self-employment as financially attractive as employee status, we believe that there is a real danger that many professional men will bypass the private practice of their profession. A shift away from individual enterprise has become noticeable in the past few years. A continuation of this situation may not only limit individual initiative but may also create a shortage of medical services in certain areas. For example, it could contribute to a maldistribution of physicians since it makes the large city more attractive to the young professional man by providing more opportunities for him to become employed. I am convinced that the enactment of this legislation would make the smaller communities of America better able to compete with the big cities for the services of physicians.

On the basis of my own observations over many years of practice in medicine, I am convinced that this is one of the factors contributing to the pronounced migration of professional people into urban areas. So, quite apart from the objective of obtaining tax equality with our employed counterparts, we urge you to approve legislation of this type, because it is in the public interest.

This legislation will be of particular benefit to physicians and other professional men who go through a long and costly period of training, and whose earnings are received in a comparatively short period of years when they are subject to high income tax rates.

Under the program proposed in the pending bill, the amount of each person's pension would be determined by his own contributions, without any funds being added by the government. In addition, the program would have the advantage of not forcing an individual into idle retirement in order to draw upon his pension fund. Most important, it presents an opportunity for the self-employed to provide for their own retirement without undue discrimination.

Because such a law will remove the existent discrimination against the self-employed citizen, the American Medical Association strongly urges its favorable consideration by your Committee.

Mr. Chairman, let me take this opportunity to thank you and the Committee for allowing us to express the views of the American Medical Association on this important measure. Dr. Archer and I will be happy to answer any questions the Committee may have.

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DR. BRAMLITT TO BE SECRETARY OF COUNCIL ON SCIENTIFIC ASSEMBLY

Dr. Charles H. Bramlitt, recently retired from the U. S. Air Force and currently Secretary of the Section on Military Medicine of the Scientific Assembly of the American Medical Association, will become a member of the staff of the American Medical Association on Aug. 1 and will work with Dr. Hull. When Dr. Hull retires as Secretary of the Council on Scientific Assembly at the end of the year Dr. Bramlitt will become Secretary.

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MEDICAL NEWS

CALIFORNIA

Ophthalmologist Honored.—A special number of the *American Journal of Ophthalmology* has been dedicated to Dr. Frederick C. Cordes, San Francisco, chairman, department of ophthalmology, University of California School of Medicine. This issue was dedicated to Dr. Cordes on the occasion of his 67th birthday and his retirement from the faculty. He has been department chairman since 1934 and a member of the U. C. Medical Center staff since earning his M.D. degree there in 1918. The issue contains tributes to Dr. Cordes' accomplishments in medical education and the study of eye diseases by several distinguished ophthalmologists and by associates in the university, including President Emeritus Robert Gordon Sproul.

Personal.—Dr. James N. Waggoner, Chicago, regional medical director for United Air Lines, has joined the Garrett Corporation's AiResearch Manufacturing Division of Los Angeles as medical director.——Dr. Howard R. Bierman resigned as director, Hospital for Blood Diseases and Medical Oncology, and scientific director, City of Hope National Medical Center, Duarte, to enter practice as a consultant in neoplastic diseases, the leukemias, and blood dyscrasias. He is establishing practice in Beverly Hills and will continue his research program. He will continue as a consultant to the City of Hope, with which he had been associated since 1953.

CONNECTICUT

University News.—Dr. Paul Howard-Flanders, of London, England, was appointed associate professor of radiology, Yale School of Medicine, New Haven. Dr. Howard-Flanders served as a lecturer in biophysics at the University of California in 1957-1958. At Yale he will conduct research in fundamental problems concerning the effect of ionizing radiation on biological systems.——Dr. Edith B. Jackson, child psychiatrist at the Yale School of Medicine, is retiring this summer after more than 25 years on the faculty. Dr. Jackson was director of the "rooming-in" project at the Yale-New Haven Medical Center from 1946 to 1951. In honor of her retirement, her colleagues and friends have given to Yale a portrait of Dr. Jackson, which will hang in the Grover F. Powers Pediatric Study of the Medical Center.

FLORIDA

International Dermatology Symposium.—An International Symposium on Griseofulvin and Dermatomycoses will be held at the University of Miami School of Medicine, Oct. 26-27. Under the sponsorship of the medical school's department of medicine, 50 American and foreign authorities will discuss the mechanism of action of Griseofulvin, its experimental toxicology, and its use in fungous diseases of the hair, skin, and nails. Among those scheduled to give papers are Dr. A. Kaminsky, Buenos Aires Medical School; Dr. F. Latapi, Medical School of Mexico City; Dr. S. C. Desai, Medical College of Bombay; and Dr. R. S. C. Aytoun and Dr. A. H. Campbell, of Glaxo Laboratories (England). The use of Griseofulvin in onychomyocosis, tinea pedis and capitis, favus, endothrix *Trichophyton* infections, and deep mycoses will be discussed, as well as laboratory, animal, and experimental studies on the drug. Information may be obtained from Dr. Harvey Blank, professor of dermatology, University of Miami School of Medicine, Miami, Fla.

State Residency Required for Miami School.—The University of Miami School of Medicine, which has previously required a seven-year residence in Florida for admission to its classes, will, beginning Aug. 6, admit students if they have legal residence in the state. This period has been set at one year by the state authorities. The law affecting the admission of students to the medical school here was changed by the State Legislature at the recent session, it was announced by Dr. Homer F. Marsh, dean of the school. By the terms of the subsidy granted to the school by the State of Florida, 90% of the student body must be residents of the state. The definition of residence has been modified so that the medical school admission requirement is now the same as that for the universities operated by the state itself. The medical school has for the past two years admitted five out-of-state residents and about 70 Floridians to each freshman class. Prior to 1957 no out-of-state applicants were admitted. The medical school, opened in 1952, graduated its first class in 1956 and now has 178 alumni. The freshman class to be admitted in September will number about 75 students. Total number of students in the school now is 270.

ILLINOIS

Mental Hospital Addition.—A preview open-house and tour of a new, 30-bed, $150,000 addition to Forest Hospital, a private mental institution, was

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

held Aug. 8 at the hospital, 555 Wilson Lane, Des Plaines. The tour included all the features of the 6,000 square foot addition, such as the solarium, patients' rooms, treatment and consultation rooms, nurses' rooms, and staff offices. Furnishings in the new private, double, and three-bed rooms include sofa beds, desks, lounge chairs, and original paintings to produce the appearance of lounges, rather than of hospital rooms. The present facilities of 50 beds will be increased to 90 with the new addition.

Chicago

Lecture by Uruguayan Physiologist.—Prof. Roberto Caldeyro-Barcia, chairman, section on obstetrical physiology, School of Medicine, Montevideo, Uruguay, will present "Recent Advances in our Knowledge on Oxytocin," Wednesday, Sept. 23, 4:30 p. m., at Dora De Lee Hall, The Chicago Lying-in Hospital, University of Chicago School of Medicine.

Dr. Newman Cited.—Dr. Louis B. Newman was the recipient of the 1959 "Citation for Public Service" from the University of Chicago. He was awarded the citation for having "accepted the privileges of a university education by assuming the obligations to society in exercising leadership in those civic, social, and religious activities that are essential to a democracy; for his public spirited citizenship and unselfish and effective service to the community, the nation, and humanity; and for the credit this service has reflected on the University and its alumni." Dr. Newman, chief of the physical medicine and rehabilitation service, Veterans Administration Research Hospital, is president of the American Academy of Physical Medicine and Rehabilitation.

INDIANA

Experimental Education Program.—Indiana University announced the appointment of Dr. Douglas A. MacFadyen, of the University of Illinois College of Medicine, Chicago, to direct its new experimental program in medical education to be inaugurated in September. The new program, "a departure and extension of traditional medical training," was announced early this year coincident with the university's receipt of a pilot grant of $173,000 by the Commonwealth Fund. Starting this fall with a limit of 10 students, selected from about 180 to be admitted to the School of Medicine, the program will draw on the resources of the College of Arts and Sciences and Graduate School and will be administered by the Medical School at Indianapolis under Dean John D. VanNuys. Eventually, 30 students at the end of their junior year in arts and sciences will be selected. "Students in the new program," it was explained by Dr. MacFadyen, "will accomplish work for an A.B. degree and then work in the six preclinical departments constituting the first two years of a medical curriculum and a broader than usual scientific and cultural training capped by an A.M. degree. Thereafter, each student may proceed in either of two directions, either to a medical career after a clinical training with or without further work in the Graduate School or to some other career in research and teaching." The new program has these objectives: a thorough training in polytechnical and cultural subjects, preparation of medical students whose paramount interests are in research and teaching, and an increase in the number of "broadly qualified" physicians. Dr. MacFadyen, also will be professor of pathology in the School of Medicine.

NEW JERSEY

Change of Address.—The new address of the Academy of Medicine of New Jersey is: Academy of Medicine of New Jersey, Library, 307-17 Belleville Ave., Bloomfield, N. J. The old address, no longer effective, was 91 Lincoln Park, Newark 2, N. J.

Survey of Nurses.—Rutgers University College of Nursing, in cooperation with the New Jersey Division of Civil Defense, will distribute a questionnaire in October to the state's 35,000 registered professional nurses to inventory their qualifications and locations and note shortages. The four-page survey has 46 questions. The study seeks to determine where nurses are employed, type of nursing performed, educational qualifications, psychiatric and public health nursing education and experience, degree of activity and income during 1959, specialized experience, postlicensing education and reasons for inactivity in the profession.

NEW YORK

New York City

Personal.—Dr. Irwin L. V. Norman was appointed medical director of The Chase Manhattan Bank. Dr. Norman served in the U. S. Navy from 1927 until April 30, when he retired with rank of rear admiral.——Dr. George M. Wheatley was appointed head of the Metropolitan Life Insurance Company's health and welfare division, succeeding Dr. William P. Shepard, who recently was appointed chief medical director of Metropolitan and placed in charge of all the company's medical and public health activities.

Dr. Ferree Named Director of Blindness Society.—Appointment of Dr. John W. Ferree as successor to Dr. Franklin M. Foote, former executive director of the National Society for the Prevention of Blindness, was announced by Ira V. Hiscock, Sc.D., the Society's president. For the past 11 years Dr. Ferree has been director of Community Service and Education and for two years associate medical director of the American Heart Association. Dr. Foote resigned recently to accept appointment as commissioner of the Connecticut State Department of Health, Hartford. The Connecticut health program is being expanded to include administration of four hospitals for chronic disease and two for mentally handicapped children.

Dr. Swan Named Anatomy Chairman.—The appointment of Dr. Roy Craig Swan Jr. as chairman of the department of anatomy has been announced by Cornell University Medical College. Dr. Swan from 1950-1952 was a research fellow in medicine, Harvard Medical School, and resident in medicine, Peter Bent Brigham Hospital, Boston. Since then he was an instructor, assistant, and then associate professor of physiology at Cornell University Medical College. He has been a Life Insurance Medical Research Fund Fellow and a Markle Scholar in Medical Sciences. He is a diplomate of the American Board of Internal Medicine.

Units for Heart Disease Patients.—Two new units of a program to advance Presbyterian Hospital's facilities for the diagnosis and surgical treatment of heart diseases have been completed. The program was facilitated by a research grant from the John A. Hartford Foundation, Inc., and is the result of three years planning by a group of Columbia-Presbyterian Medical Center anesthesiologists, surgeons, cardiologists, and radiologists. The cardiac special care unit is a recovery room for patients who have undergone heart surgery. The unit is staffed by nurses with experience in the postoperative care of this type of patient and fills the need of providing intensive care over a period of several days. Each of the five beds has its own battery of equipment for constant monitoring of the patient's recovery. The diagnostic unit includes a modern angiocardiography room which will more than double Presbyterian Hospital's facilities for caring for cardiac patients.

OKLAHOMA

Doctors Building Opened.—The new seven-story Doctors Building at 21st and Lewis Streets, in Tulsa, was opened in June. Erected at a cost of $1,500,000, the structure provides offices for 53 physicians and four dentists. Among the facilities in the new building are two radiology laboratories, three pathology and bacteriology laboratories, a pharmacy, optician, and coffee shop. Work on the 65,000 square foot unit which was begun 15 months ago was financed by its tenants through the self-owned Twenty-first Street Building Corporation. The building has walls of insulated procelain steel panels, with structural columns and windows covered with aluminum. It is completely air-conditioned and uses a specially engineered type of heating equipment to meet the needs of multiple examination and treatment rooms. Each suite is designed to the individual requirements of the tenant. A parking area east of the building provides parking for patients and visitors. A second lot located west, across Lewis Avenue accommodates cars of doctors and office personnel.

Dr. Turner Named Schering Scholar.—The Endocrine Society named Dr. Henry H. Turner, Oklahoma City, as this year's Schering Scholar. The award was presented to Doctor Turner during June 5 ceremonies held in conjunction with the annual meeting of the organization in Atlantic City. An anonymous committee of the Council of the society selected Dr. Turner for the $2,500 grant on the basis of his accomplishments as an established investigator in the fields of endocrinology. The cash award is made possible by the Schering Corporation and is presented annually to a "deserving physician who wishes to extend the opportunities for his work either here or abroad." Dr. Turner has announced that he intends to utilize the grant by attending both the 1960 International Goiter Conference, London, and the International Congress of Endocrinology, to be held in Copenhagen the same year. While abroad, he will also visit with a number of European investigators. In addition to being the Schering Scholar, he holds the office of secretary-treasurer for the national organization and is president of the National Society of Nuclear Medicine.

OREGON

Meeting on General Practice in Portland.—The Oregon Academy of General Practice will present "Horse and Buggy Doctor" as the 12th annual scientific session of the Northwest Regional Academy meeting, Sept. 9-11, at the Portland State College, Portland. Dr. Howard A. Rusk, chairman, department of physical medicine and rehabilitation, New York University-Bellevue Medical Center, and Dr. Edward H. Rynearson, chairman, section on metabolic diseases, Mayo Clinic, Rochester, *Minn.*, will be the Sommer Memorial Lecturers. Other speakers include the following: Drs. A. Cannon Eley, Boston; L. Henry Garland, San Francisco; Ian MacDonald, Los Angeles; John O. McCall Jr., Portland; Leland S. McKittrick, Brookline, Mass.; Frank W. Norman, Santa Rosa, Calif.; Richard H. Overholt, Boston; Robert H. Tinker, Portland; and Roger H. L. Wilson, San Francisco. At the annual banquet Sept. 10, 7:30 p. m., Dr. Fount Richardson, Fayetteville, Ark., president, American Academy of General Practice, will be the speaker. Exhibits are planned, and entertainment includes a cruise and deep-sea fishing. The program has been approved for 15 hours of category I credit. There is no registration fee. The theme "Horse and Buggy Doctor," was selected to celebrate Oregon's 100th birthday as a state. For information write Mrs. Thomas Sterm, Chairman, Advance Registration Committee, Route 4, Sherwood, Ore.

PENNSYLVANIA

Philadelphia

Dr. Koprowski Awarded Alvarenga Prize.—On July 14, the College of Physicians of Philadelphia awarded the Alvarenga Prize for 1959 to Dr. Hilary Koprowski, professor of research medicine, University of Pennsylvania, "for his outstanding work on the development of a living attenuated virus vaccine against poliomyelitis." The Alvarenga Prize was established by the will of Pedro Francisco DaCosta Alvarenga, of Lisbon, Portugal, an associate fellow of the College of Physicians of Philadelphia, to be awarded annually by the college on the anniversary of the death of the testator, July 14, 1883.

Personal.—At the 60th annual meeting of the American Gastroenterological Association Dr. Russell S. Boles was presented with the Julius Friedenwald Medal, awarded each year to a member of the association "for outstanding achievement in gastroenterology." ——Dr. Gordon N. French, of Brookline, Mass., was appointed director of internal medicine at Misericordia Hospital. Dr. French was formerly on the faculty of medicine at Tufts University Medical School and a research associate in physiology at Harvard School of Public Health.

Teaching and Research Center.—The development of a new integrated teaching and research center for the basic biological sciences at the University of Pennsylvania, to be closely associated with the university's School of Medicine, was made possible by three grants totaling $1,903,345. Grants of $1,000,000 from the Longwood Foundation, a philanthropic organization created by Pierre S. duPont; $473,345 from the U. S. Public Health Service; and $430,000 from the Rockefeller Foundation will bring into being a new building for the university's division of biology, directed by David R. Goddard, Ph.D., Gustave C. Kuemmerle Professor of Botany. Several levels will interconnect with the Medical School's research building. The grants also make possible rehabilitation of portions of an existing zoology building, to which the new structure will be joined, and provide construction of greenhouses and a service laboratory. The building will be adjacent to the School of Medicine's new medical research building under construction on Hamilton Walk. The new air-conditioned biology building will be about 36,000 square feet in area and will include lecture and seminar rooms, a biological library, teaching laboratories, and research rooms. The new 4,000-square-foot service laboratory, which will connect with the remodeled zoology building, will contain air-conditioned animal quarters and climatically and atmospherically controlled experimental plant growth chambers. Construction of the biology building, renovation of the zoology building, and construction of the adjacent structures will accomplish the university's goal of physical integration of the division of biology. The division was organized in 1957 through academic and administrative integration of the earlier departments of botany, zoology, and microbiology of the College of Arts and Sciences.

SOUTH CAROLINA

Hospital Dedicated in Charleston.—Dedication ceremonies for the new McClennan-Banks Memorial Hospital on Courtenay Drive, Charleston, were held on May 31. The 31-bed hospital, which cost $686,000 in county and federal funds, is now open for patients. It has one private room, 11 two-bed rooms, and two four-bed wards and a conference room. Dr. Thomas C. McFall, administrator of the new hospital, has been a leader in efforts to establish a new unit as a replacement for the old Negro Hospital and Training School on Cannon Street. The hospital is named in honor of Dr. Alonzo Clifton McClennan and Mrs. Anna D. Banks. Dr. McClennan helped found the old Negro center and served as its medical director and surgeon until his death in 1912. He was a native of Columbia and a graduate of Howard University schools of pharmacy and medicine. Mrs. Banks was the first head nurse of the old Hospital and Training School and later became superintendent of nurses. She died in 1930.

TEXAS

Dr. May Owen Honored.—Dr. May Owen of Fort Worth, Texas, was elected president-elect of the Texas Medical Association. She will be the first woman to hold the office of president in the association's 106-year history. Dr. Owen was the first woman president of the Tarrant County Medical Society and is a past-president of the Texas Society of Pathologists.

UTAH

Annual Scientific Session.—The 64th annual scientific session of the Utah State Medical Association will be held Sept. 16-18 at the Hotel Utah Motor Lodge, Salt Lake City. Dr. Ulrich R. Bryner, Salt Lake City, president of the association will open the session with an address. Two symposiums are planned: "Newer Adrenocorticosteroids," moderated by Dr. Frank H. Tyler, and "Basic Principles and Care of Hand Injuries," moderated by Dr. Thomas R. Broadbent. The program will include papers by the following out-of-state speakers: Drs. Edward L. Bortz, Philadelphia; Thomas McPherson Brown, Washington, D. C.; Charles R. Stephen, Durham, N. C.; James R. Willson, Philadelphia; Phillips Thygeson, San Jose, Calif.; James W. Littler, New York City; John L. Emmett, Rochester, Minn.; and Reginald H. Smithwick, Boston. An informal panel discussion moderated by Dr. John F. Waldo, president, Salt Lake County Medical Society, is planned for the luncheon of Sept. 16. Specialty group discussions will be held the evening of Sept. 17. Dr. Louis M. Orr, Orlando, Fla., President, American Medical Association, will be the speaker at the president's banquet, 7:30 p. m., Sept. 18, presenting, "Medicine Is Not Failing America." For information write Mr. H. Bowman, 42 S. 5th East, Salt Lake City, Executive-Secretary.

WASHINGTON

Annual Convention in Seattle.—The 70th annual session of the Washington State Medical Association will be held Sept. 13-16, at the Olympic Hotel, Seattle. Dr. E. Vincent Askey, Los Angeles, President-Elect, American Medical Association, will be the featured speaker in the nonscientific program of the convention. Guest scientific speakers are: Drs. Lawson Wilkins, Baltimore; Carleton Mathewson Jr., San Francisco; John Shea, Memphis, Tenn.; Robert H. Williams, Seattle; and Frank C. Winter, Palo Alto, Calif. There will be Monday and Tuesday morning sessions with special subject matter in the following fields: pediatrics; internal medicine; ear, nose, and throat; surgery; and eye. General scientific sessions will be held in the afternoon. The scientific program will climax with a general scientific session the morning of Sept. 16 and a limited attendance seminar, "Electrolyte and Fluid Management Problems." President of the association is Dr. Emmett L. Calhoun of Aberdeen. For information, write Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

GENERAL

Psychosomatic Meeting in Cleveland.—The sixth annual meeting of the Academy of Psychosomatic Medicine will be held Oct. 15-17, at the Sheraton–Cleveland Hotel, Cleveland. The meeting will be oriented and directed to fit the needs of nonpsychiatric physicians. Practical everyday office management of psychosomatic problems and emotional disturbances will be dealt with in formal papers, symposiums, panel discussions, and small study groups. The meeting will be open to all scientific disciplines, as well as psychologists, social workers, and nurses. Information may be obtained from Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2.

Society News.—At the 70th annual meeting of the **American Dermatological Association, Inc.**, in Atlantic City, Dr. Marion B. Sulzberger, of New York City, was elected president for the coming year, and Dr. Lawrence G. Beinhauer, of Pittsburgh, vice-president. Dr. Carl T. Nelson, of New York City, is treasurer, and Dr. Wiley M. Sams of Miami, Fla., secretary. The next annual meeting of the association will be held at the Boca Raton Hotel and Club, Boca Raton, Fla., April 8-12, 1960. —The officers of the **American Proctologic Society** for the year 1959-1960 are: president, Dr. Hyrum R. Reichman, Salt Lake City; president-elect, Dr. Walter A. Fansler, Minneapolis; vice-president, Dr. Neil W. Swinton, Boston; secretary, Dr. Norman D. Nigro, Detroit; and treasurer, Dr. Robert J. Rowe, Dallas, Texas. The next annual meeting will be held April 25-27, 1960, at the Shamrock Hilton Hotel in Houston, Texas.

Mississippi Valley Meeting.—The 24th annual meeting of the Mississippi Valley Medical Society will be held at the Chase Hotel, St. Louis, Sept. 29-Oct. 1, under the presidency of Dr. Arthur F. Fritchen, of Decorah, Iowa. The morning and afternoon sessions on Sept. 29 will be devoted to clinics held in the teaching hospitals of St. Louis and Washington University schools of medicine. A joint meeting with the St. Louis Academy of General Practice and the St. Louis Dental Society will be held the evening of Sept. 29, with the opening of the industrial and scientific exhibits at 6:00 p. m. on that day. Over 30 clinical teachers are on the program. In addition, the program includes Dr. Jacob A. Bargen, Rochester, Minn.; Dr. Lester R. Dragsredt, Chicago; Dr. E. Grey Dimond, Kansas City, Kan.; Dr. J. P. Greenhill, Chicago; Dr. Heyworth N. Sanford, Chicago; and Dr. Robert L. Jackson, Columbia, Mo.; Dr. Harvey Flack of London, England, will be the banquet speaker. There will be panel discussions on pediatric heart problems, surgery in peptic ulcer, heart disease and atherosclerosis, and highway injuries. A complete program may be obtained from Dr. Harold Swanberg, Secretary, W.C.U. Bldg., Quincy, Ill. (The meeting will be followed by the 16th annual meeting of the American Medical Writers' Association at the Chase Hotel, Oct. 2-3.)

Rocky Mountain Medical Conference.—On Sept. 8-11, at the Shirley–Savoy Hotel, Denver, the 10th biennial Rocky Mountain Medical Conference will be held in combination with the 89th annual session of the Colorado State Medical Society. The conference is a joint enterprise of the Colorado, Montana, New Mexico, Utah, and Wyoming state medical societies. Guest speakers at the conference are as follows: Drs. Edward L. Bortz, Philadelphia; Harold W. Dargeon, New York; Fred C. D. Collier, Birmingham, Ala.; M. Edward Davis, Chicago; L. Henry Garland, San Francisco; L. Stanley James, New York; Theodore G. Klumpp, New York; Ben M. Peckham, Madison, Wis.; Jack Weinberg, Chicago; and Danely P. Slaughter, Chicago. Three closed circuit television clinics are planned: "Ob-Gyn and Pediatrics," "Leukemias and Lymphomas," and "Care and Rehabilitation of the Older Patient." Scientific and technical exhibits are planned. A program of entertainment and special events is arranged. A banquet will be held Sept. 10, at 7:30 p. m. Registration fee is $5. For information write Mr. Harvey T. Sethman, Executive Secretary, Colorado State Medical Society, 835 Republic Building, Denver 2.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	July 25, 1959		July 26, 1958 Total
	Paralytic Type	Total Cases	
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	2	3	..
Rhode Island	..	..	1
Connecticut	1	1	..
Middle Atlantic States			
New York	7	7	6
New Jersey	2	2	10
Pennsylvania	7	9	4
East North Central States			
Ohio	4	9	8
Indiana	4	7	6
Illinois	2	6	3
Michigan	1	5	4
Wisconsin	..	1	1
West North Central States			
Minnesota	3	5	..
Iowa	6	20	..
Missouri	14	18	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	5	8	1
Kansas	2	8	1
South Atlantic States			
Delaware	1	1	1
Maryland	..	..	..
District of Columbia	..	..	1
Virginia	8	9	8
West Virginia	3	3	6
North Carolina	8	11	4
South Carolina	..	2	4
Georgia	1	1	1
Florida	5	8	3
East South Central States			
Kentucky	..	..	..
Tennessee	11	13	..
Alabama	20	24	1
Mississippi	1	2	3
West South Central States			
Arkansas	10	13	..
Louisiana	10	13	5
Oklahoma	5	8	4
Texas	15	31	28
Mountain States			
Montana	..	1	4
Idaho	..	1	1
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	1	1	..
Arizona	1	3	..
Utah	..	..	2
Nevada	1	1	..
Pacific States			
Washington	..	1	2
Oregon	4	5	..
California	11	13	9
Alaska	1	1	..
Hawaii	..	..	3
Territories and Possessions			
Puerto Rico	..	..	1
Total	177	278	136

Care of Child with Rheumatic Fever.—A new booklet, "Home Care of the Child with Rheumatic Fever," was published by the American Heart Association and its affiliates. The booklet was prepared especially for parents of children who have rheumatic fever or are recovering from it and for whom hospital care is either not advised or not available. Copies may be requested by physicians and others from local heart associations to give to parents of rheumatic fever patients. The 24-page illustrated booklet gives details about the role of the mother in caring for the sick child and the importance of following the regimen prescribed by the physician. Instruction is included on bathing the child in bed, giving medicine, taking the pulse and temperature, and keeping records.

Red Cross Adopts Mouth-To-Mouth Lifesaving Method.—The American Red Cross officially adopted the mouth-to-mouth technique of artificial respiration for adults as well as children. Teaching of the method in Red Cross first aid and water safety courses will begin immediately. The technique was declared the most practical in a unanimous verdict of a committee of the National Academy of Sciences—National Research Council after a thorough review of artificial respiration data. The Red Cross delayed announcement of its adoption of the method only long enough to prepare and have published an instruction manual for use of its volunteer class instructors. Distribution of copies of this manual to the 3,700 Red Cross Chapters was completed early in July. The Red Cross still considers manual methods of artificial respiration acceptable for rescuers who cannot or will not use the mouth-to-mouth or mouth-to-nose technique. The two methods it recommends are the Nielsen back pressure-arm lift method and the Silvester chest pressure-arm lift method.

LATIN AMERICA

Research in Genetics by Brazilian Scientists.—Four Brazilian universities and the Brazilian Society of Genetics are cooperating in a major new program of research in human genetics with the help of five Rockefeller Foundation grants totaling $120,250. Brazilian geneticists have already made distinguished collaborative research on Drosophila population genetics. Their new cooperative program in human genetics will be planned primarily by the Brazilian Society of Genetics. The University of São Paulo is the first Brazilian school to offer a course in human genetics to medical students, and the first to develop a broad research program in the field. Research in human genetics already in progress at the University of Paraná, Curitiba, includes a study of consanguineous marriages in several Brazilian states. The University of Rio Grande do Sul, in Porto Alegre, will establish a human serum bank where antisera will be available to all investigators. Genetic studies on several Indian tribes, including one in an isolated region of the Amazon Basin, will be done by the University of Bahia in Salvador.

CORRECTION

Polyps of the Colon and Rectum.—In the article "Polyps of the Colon and Rectum" by Rider et al. (in THE JOURNAL, June 6, page 633) the term adenocarcinoma was used throughout in place of the term adenoma malignum, to agree with the terminology preferred in the fourth edition of Standard Nomenclature of Diseases and Operations. The authors have now stated that throughout their paper the meaning of adenocarcinoma is adenocarcinoma grade 1, or the synonyms adenocarcinoma in situ or adenoma malignum.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications was June 22. Succeeding examinations—March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23, 1960. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Examination.* Phoenix, Oct. 14-16. *Reciprocity.* Phoenix, Oct. 17. Ex. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

Arkansas:* *Examination and Reciprocity.* Little Rock, Nov. 5-6. Sec., Dr. Joe Verser, Harrisburg.

California: *Written.* Sacramento, October 19-22. *Oral.* Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Connecticut:* *Homeopathic. Examination.* Derby, Sept. 8. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

District of Columbia:* *Examination.* Washington, Dec. 14-15. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Florida:* *Examination.* Miami Beach, Nov. 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, Oct. 13. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity.* Kansas City, January 1960. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Louisiana: *Examination and Reciprocity.* New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maryland: *Examination.* Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Minnesota:* *Examination and Reciprocity.* St. Paul, Oct. 20-22. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

Montana: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

Nevada:* *Examination and Reciprocity.* Reno, Sept. 8. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

New Hampshire: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

New Jersey: *Examination.* Trenton, Oct. 20-23, *Reciprocity.* Monthly, Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

New Mexico:* *Examination and Reciprocity.* Santa Fe, Nov. 16-17. Sec., Dr. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination.* Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

Ohio: *Examination.* Columbus, Dec. 15-17. *Endorsement.* Columbus, Aug. 26 and Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

Oregon:* *Examination.* Portland, Oct. 22-24. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

Puerto Rico: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Tennessee:* *Examination.* Memphis, Sept. 23-24. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

Texas:* *Examination.* Fort Worth, Dec. 3-5. *Reciprocity.* Houston, Aug. 29-31. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Virginia: *Examination and Reciprocity.* Richmond, Dec. 2-4. Address: Board of Medical Examiners, 631 First St. S.W., Roanoke.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 5. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination and Reciprocity.* Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

Arizona: *Examination.* Tucson, Sept. 15. Sec., Mr. Herman E. Bateman, University of Arizona, Tucson.

Colorado: *Examination.* Denver, Sept. 2-3. *Reciprocity.* Denver, Sept. 4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, Oct. 10. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

District of Columbia: *Examination.* Washington, Nov. 23-24. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Kansas: *Examination.* Pittsburg, Nov. 6-7. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 9-10. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Minnesota: *Examination.* Minneapolis, Oct. 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

Nevada: *Reciprocity*, Sept. 8. Sec., Dr. Kenneth C. Kemp, Box 9355, University of Nevada, Reno.

New Mexico: *Reciprocity.* Santa Fe, Oct. 7. Sec., Mrs. M. Cantrell, P. O. Box 1522, Santa Fe.

Oklahoma: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

South Dakota: *Examination.* Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Texas: *Examination.* Austin, Oct. 12-13. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 11 and Milwaukee, Dec. 5, Sec., Mr. Wm. H. Barber, 621 Ranson St., Milwaukee.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

ARMY

Dr. Sim Honored.—Dr. Van M. Sim, chief of the Chemical Warfare Laboratories' clinical research division at Army Chemical Center, Maryland, was given the Army's highest civilian award, the Decoration for Exceptional Civilian Service. Dr. Sim was cited for "volunteering to be the first to expose himself to several new chemical agents at the risk of grave personal injury and the direction of a program whereby over 400 volunteers have been exposed without a single injury."

Personal.—Col. James T. McGibony, M. C., was appointed chief of the medical plans and operations division in the office of the surgeon general thereby succeeding Col. Angel A. Cardona, M. C., who is now surgeon of the military district of Washington.

NAVY

Personal.—Capt. Clifford P. Phoebus, M.C., U. S. Navy, recently reported to the Bureau of Medicine and Surgery for duty as director, Astronautical Division.

VETERANS ADMINISTRATION

Personal.—Dr. Frederick J. Rachiele, formerly director of professional services at the Veterans Administration hospital in Denver, Colo., wa appointed manager of the Tucson, Ariz., VA hospital.

PUBLIC HEALTH SERVICE

Directory of Research Fellows.—The National Cancer Institute has published the first directory of its research fellows since the fellowship program was established in 1937. Section 1 of the directory contains the names of 924 persons whose fellowships were completed prior to April 1, 1958, and section 2 contains the names of 245 persons whose fellowships extended beyond that date. A brief statement about each fellow tells the highest degree he held at the time of his appointment, the name of the school granting the degree, the type, duration, and place of his fellowship, and the name of the research project. The present position of those whose fellowships had terminated by April 1, 1958, is also given. The introduction to the directory discusses the history of the program, which was the first of its kind to be supported by the federal government.

Most of the former fellows are now engaged in research or teaching or both. About half of the fellows appointed in the early years of the institute are now permanent members of the institute's staff in key research positions, and a number of the later fellows have also joined the staff. Copies of the directory (Research Fellows of the National Cancer Institute, 1938-1958) were sent to the libraries of appropriate institutions, including four-year colleges, medical schools, and foundations supporting research. Copies are also on sale by the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 45 cents a copy.

Appointments to Selection Committee for Senior Research Fellowships.—Drs. Kimball C. Atwood, of the department of obstetrics and gynecology at the University of Chicago; Howard C. Hopps, chairman of the pathology department at the University of Texas; Eli D. Goldsmith, professor of histology and research coordinator at New York University College of Dentistry; Antonio Ciocco, head of the department of biostatistics at the University of Pittsburgh's Graduate School of Public Health; and John B. Graham, professor of pathology at the University of North Carolina, were appointed to serve three-year terms on the selection committee for the Senior Research Fellowship program of the National Institutes of Health. They will advise and make recommendations to the surgeon general on the selection of qualified persons for the five-year fellowships. The fellowship awards are designed principally for promising young scientists sponsored by preclinical departments in the period between the completion of their postdoctoral research training and their eligibility for permanent higher academic appointments. Under special circumstances, senior scientists may be awarded these fellowships to supply needed strength in preclinical science departments.

Personal.—Dr. Henry S. Kaplan, professor of radiology at Stanford University School of Medicine, and Dr. Stanhope Bayne-Jones, well-known medical educator, were appointed to four-year terms as members of the National Advisory Cancer Council, effective Oct. 1. In this capacity they will advise and make recommendations to the surgeon general regarding research activities of the National Cancer Institute. The council is composed of 12 members, 6 of whom are leaders in science and 6 leaders in education and public affairs.

FEDERAL AVIATION AGENCY

Civil Air Surgeon Appointed.—Dr. James L. Goddard was appointed civil air surgeon of the Federal Aviation Agency. He is the first to hold this title, although the post had been filled on an acting basis by Dr. John E. Smith. Dr. Smith is now chief of the research requirements in the office of the civil air surgeon. The civil air surgeon is concerned with the mental and physical fitness of airmen and air traffic controllers and the chief of the research requirements division is responsible for the application of findings of aeromedical research to civil aviation.

DEATHS

Bauer, Wesley Warren Ⓜ Fort Morgan, Colo.; (licensed in Colorado in 1920); died May 31, aged 64.

Benson, Theodore J. Ⓜ Fromborg, Mont.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; served as mayor and member of the school board; died in the Deaconess Hospital, Billings, June 2, aged 85.

Bronson, Malcolm Ⓜ Hamilton, Ohio; Miami Medical College, Cincinnati, 1908; died May 31, aged 74.

Buckingham, Edwin Wheeler II Ⓜ Newport News, Va.; Medical College of Virginia, Richmond, 1918; veteran of World War I; served as a medical missionary in China; associated with the Riverside Hospital, where he was secretary-treasurer of the medical staff from 1931 to 1947; recently honored as the city's Doctor of the Year; died June 6, aged 66.

Canright, Harry Lee, St. Cloud, Fla.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1889; for many years a medical missionary in China; died May 28, aged 94.

Clauser, Eldo Horace Mann Ⓜ Muncie, Ind.; born in Owasco, Ind., March 27, 1890; Indiana University School of Medicine, Indianapolis, 1915; past-president and charter member of the Muncie Academy of Medicine; past-president of the Delaware–Blackford Counties Medical Society; fellow of the American College of Surgeons, of which he was a member of the board of governors from 1955 to 1958, and a past-president of the Indiana Chapter; served as chairman of the executive committee and member of the council of the Indiana State Medical Association; founding member of the U. S. Committee of the World Medical Association; since its inception, chairman of the Indiana Hospital Licensing Committee; veteran of World War I; a member of the board of governors of the Blue Shield; a member of the board of directors of the local YMCA; past-president of the Muncie Kiwanis Club and the local Indiana University Alumni Association; for many years chairman of the executive committee of the staff of Ball Hospital, where he died May 31, aged 69.

Cooney, M. Blanche Ⓜ West Newbury, Mass.; Tufts College Medical School, Boston, 1911; served on the staff of the Hale Hospital in Haverhill; died May 23, aged 69.

Culbertson, Ora J. Ⓜ Belleville, Ill.; St. Louis University School of Medicine, 1902; fellow of the American College of Surgeons; associated with the St. Mary's and Christian Welfare hospitals; died May 29, aged 81.

Driskell, Cecil Rogers Ⓜ Springfield, Ill.; St. Louis University School of Medicine, 1906; past-president of the Montgomery County Tuberculosis Association; died in St. John's Hospital May 20, aged 74.

Gallagher, James S. Ⓜ St. Petersburg, Fla.; Temple University School of Medicine, Philadelphia, 1909; for many years practiced in Philadelphia; died in the Episcopal Hospital, Philadelphia, June 4, aged 74.

Gallaspy, Glenn Todd Ⓜ West Monroe, La.; Emory University School of Medicine, Atlanta, 1931; associated with St. Francis Hospital in Monroe, where he died May 30, aged 51.

Gerstner, David, Kansas City, Mo.; Eclectic Medical University, Kansas City, 1918; died May 28, aged 80.

Ghormley, Ralph Kalb Ⓜ Carmel, Calif.; born in Portland, Ore., Feb. 10, 1893; Johns Hopkins University School of Medicine, Baltimore, 1918; following service as a medical officer with the American Expeditionary Forces, interned at Johns Hopkins Hospital and Children's Hospital in Baltimore and the New York Hospital in New York City; in 1921-1922 assistant resident surgeon at Johns Hopkins Hospital in Baltimore; entered the practice of orthopedic surgery in Boston, where in 1922-1923 he was an assistant in orthopedic surgery at Harvard Medical School, and later an instructor; served as attending orthopedic surgeon to the Massachusetts General Hospital in Boston; came to Rochester, Minn., in September, 1929, as a consultant in orthopedic surgery at the Mayo Clinic and assistant professor in Mayo Foundation, Graduate School, University of Minnesota; advanced to associate professor in 1932 and full professor in 1937 and, in 1938, became head of the orthopedic section of the Mayo Clinic, a post he held until 1955, when he became a senior consultant; specialist certified by the American Board of Orthopedic Surgery, of which he was past-president; past-president and secretary of the American Orthopedic Association; past-president of the Clinical Orthopaedic Society; elected president of the staff of the Mayo Clinic in 1952 and served as president of the Mayo Foundation Chapter of the Society of the Sigma Xi in 1943-1944; member of the Western Surgical Association, American Academy of Orthopedic Surgeons, American Association for the Sur-

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Ⓜ Indicates Member of the American Medical Association.

gery of Trauma, the Robert Jones Orthopedic Society, International Society of Orthopedic Surgery and Traumatology, the Alpha Omega medical honor society, the Harvard Club of Boston, and the Alumni Association of the Mayo Foundation; a corresponding member of the Scandinavian Orthopedic Society; fellow of the American College of Surgeons; in 1954 received a certificate of merit from the American Medical Association for an exhibit on Primary Tumors of the Soft Tissues of the Extremities Exclusive of Epithelial Tumors—An Analysis of 500 Consecutive Cases and in 1956 received a certificate of merit for exhibit on Bone Tumors; served on the staffs of the St. Mary's and Colonial hospitals in Rochester, Minn.; a consultant in his specialty to the U. S. Veterans Administration; served as a member of the advisory committee of the Children's Bureau of the U. S. Department of Labor; in 1942 gave the William J. Mayo Clinic Lecture at the University of Michigan in Ann Arbor; in 1957 was honored by former fellows in orthopedic surgery of the Mayo Foundation and colleagues at the Mayo Clinic with the establishment of the Ralph K. Ghormley Traveling Scholarship; joint author of "Diagnosis in Joint Disease: a Clinical and Pathologic Study of Arthritis"; editor of a volume "Orthopedic Surgery" published in 1938; associated with Monterey (Calif.) Hospital and the Peninsula Community Hospital, where he died June 6, aged 66.

Glasener, Charles F., Bradenton, Fla.; Loyola University School of Medicine, Chicago, 1916; for many years on the staff of the Elmhurst (Ill.) Community Hospital; died in the Manatee Veterans Memorial Hospital May 28, aged 76.

Glickman, Abraham Jacob Ⓜ Boston; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1904; died April 27, aged 80.

Greer, Charles Edward Ⓜ Charleston, Ill.; Chicago Homeopathic Medical College, 1898; veteran of World War I; member of the honorary staff of the Charleston Community Memorial Hospital, where he died June 1, aged 84.

Griffin, Silas Ⓜ St. Petersburg, Fla.; Kentucky University Medical Department, Louisville, 1900; for many years practiced in Henderson, Ky.; served as secretary of the Henderson County (Ky.) Medical Society and health officer of Henderson County; died in St. Anthony Hospital May 25, aged 83.

Hahn, Charles David, Baltimore; Medical College of Ohio, Cincinnati, 1897; died June 4, aged 86.

Hanley, James Leo Ⓜ Bridgeport, Conn.; Yale University School of Medicine, New Haven, 1935; certified by the National Board of Medical Examiners; interned at University Hospitals in Cleveland; served a residency at the Woman's Hospital in Detroit; formerly a fellow at the Mayo Foundation in Rochester, Minn.; veteran of World War II; associated with Bridgeport Hospital and St. Vincent's Hospital, where he died May 31, aged 49.

Harris, Abraham J. Ⓜ Newton, Mass.; Mid-West Medical College, Kansas City, Mo., 1934; died May 30, aged 66.

Hathaway, Alfred H. Ⓜ Mountain View, Okla.; University of Arkansas School of Medicine, Little Rock, 1905; died May 25, aged 87.

Heitmann, Kenneth Arnold Conrad Ⓜ Santa Ana, Calif.; University of Michigan Medical School, Ann Arbor, 1935; specialist certified by the American Board of Radiology, Inc.; member of the American College of Radiology; died May 26, aged 49.

Hickman, John Samuel Ⓜ Meridian, Miss.; Mississippi Medical College, Meridian, 1911; served as a member of the state legislature; for many years superintendent of the East Mississippi Hospital; died in the Rush Memorial Hospital May 31, aged 75.

Holt, Robert Edward Lee, Portland, Ore.; University of Oregon Medical School, Portland, 1908; served on the staff of the Providence Hospital, where he died June 1, aged 78.

Kass, Paul, Miami Beach, Fla.; University of Virginia Department of Medicine, Charlottesville, 1928; died in North Miami May 26, aged 56.

Kitchens, Orren William Ⓜ Byromville, Ga.; Atlanta Medical College, 1915; vice-chairman of the Dooly County Board of Commissioners; member of the city council for 42 years; on the staff of the Riverside Hospital in Montezuma; a director of the Byromville Bank; died in the Montezuma (Ga.) Hospital June 1, aged 67.

Koll, Irvin Sunthimer, Beverly Hills, Calif.; Rush Medical College, Chicago, 1907; specialist certified by the American Board of Urology; member of the American Urological Association; formerly practiced in Chicago, where he was associated with the Michael Reese Hospital, where in 1956 he was awarded a bronze plaque for at least 30 years service; author of "How to Stay Healthy"; died May 30, aged 75.

Kuykendall, Pere Moran Ⓜ Ranger, Texas; Baylor University College of Medicine, Dallas, 1917; past-president of the Eastland County Medical Society; veteran of World War I; served as medical director of the West Texas Hospital; past-president of the Chamber of Commerce, Eastland County Water Board, and Rotary Club; served as a member and president of the Eastland County School Board; died in the Ranger General Hospital May 28, aged 66.

Lang, Charles Albert, New York City; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1898; retired assistant attending in pediatrics at the Presbyterian Hospital, where he died June 1, aged 83.

Leach, Charles Henry Ⓜ Tenants Harbor, Maine; Medical School of Maine, Portland, 1899; died in Rockland May 25, aged 85.

Levy, Simon Cuthbert, Plaquemine, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1897; associated with the Plaquemine Sanitarium, where he died June 1, aged 86.

Linsin, Ivan M., St. Petersburg, Fla.; Bennett Medical College, Chicago, 1910; formerly associated with the Indian Service; died in Tampa May 29, aged 72.

Luce, Rey Vincent Ⓜ Santa Rosa, Calif.; Rush Medical College, Chicago, 1913; fellow of the American College of Surgeons; veteran of World War I; formerly practiced in Akron, Ohio, where he was chief of staff at Akron City Hospital; past-president of the Summit County (Ohio) Medical Society; died in Boyes Springs, May 30, aged 71.

Marchman, Oscar Milton Ⓜ Dallas, Texas; born in Jefferson, Texas, April 5, 1872; Missouri Medical College, St. Louis, 1899; also a pharmacist; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served as secretary of the Texas Ophthalmological and Otolaryngological Society; first president of the Dallas Academy of Medicine, which he helped organize; past-president of the Dallas Southern Clinical Society and the Dallas Academy of Ophthalmology and Otolaryngology; oldest active member of the Dallas County Medical Society, of which he was past-president, was recently given the "Golden Deeds" award by the Dallas Exchange Club for his "unselfish service"; emeritus professor of otolaryngology, Southwestern Medical School of the University of Texas; formerly on the faculty of the Baylor University College of Medicine; at one time secretary of the city board of health; past-president of the Dallas chapter of the American Red Cross; helped organize the Dallas Health and Science Museum, of which he was a trustee; associated with the Baylor University Hospital, Medical Arts Hospital, and Children's Medical Center; died in the Baylor University Hospital May 25, aged 87.

Mathers, James Andrew, Kingston, N. Y.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1917; veteran of World War I; member of the staffs of the Kingston and Benedictine hospitals; died May 19, aged 65.

Matthews, Charles B. Ⓜ Hammond, Ind.; Kentucky School of Medicine, Louisville, 1894; veteran of World War I; associated with St. Margaret Hospital; died May 30, aged 86.

Nicholls, James Benton Ⓜ Windsor, N. C.; University of Maryland School of Medicine, Baltimore, 1910; member of the American Trudeau Society; in February, 1953, a new building at the Catawba Sanatorium was named in his honor and later that year he retired as superintendent and medical director, after many years of service; died May 15, aged 71.

Noe, Carl Abraham Ⓜ Cedar Rapids, Iowa; State University of Iowa College of Medicine, Iowa City, 1929; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; served as secretary treasurer of the Iowa Academy of Ophthalmology and Otolaryngology; veteran of World War II; associated with Methodist Hospital, St. Luke's Hospital, where he was president-elect of the staff, and the Mercy Hospital, where he died May 26, aged 54.

Philp-Bradshaw, Martha, San Francisco; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1902; for many years a medical missionary in China; died May 29, aged 89.

Powell, Eppie Clifton, Middlesex, N. C.; University of Nashville (Tenn.) Medical Department, 1907; chairman of the Nash County Board of Health and Middlesex School Board; for many years physician to the Free Will Baptist Orphanage; a director of Peoples Bank & Trust Company; past-president of the Middlesex Rotary Club; died in the Wayne Memorial Hospital, Goldsboro, May 26, aged 75.

Ray, Fred Merton Ⓜ Pocatello, Idaho; Northwestern University Medical School, Chicago, 1909; veteran of World War I; associated with St. Anthony Hospital and Bannock Memorial Hospital, where he died May 29, aged 77.

Roark, Jesse Lawrence, Albuquerque, N. M.; born in Water Valley, Miss., Sept. 30, 1895; Jefferson Medical College of Philadelphia, 1924; served overseas during World War I; interned at the Jefferson Medical College Hospital in Philadelphia and served a residency at the White Haven Sanitorium in White Haven, Pa.; at one time on the teaching staff of his alma mater; formerly medical director of Lafayette and Yalobusha counties in Mississippi; served on the staffs of the Mississippi State Sanatorium for Tuberculosis in Sanatorium, Pennsylvania State Sanatorium for Tuberculosis in South Mountain, Pa., Essex County Sanatorium for Tubercular Diseases in Verona, N. J., and the Arkansas gery of Trauma, the Robert Jones Orthopedic Society, International Society of Orthopedic Surgery and Traumatology, the Alpha Omega medical honor society, the Harvard Club of Boston, and the Alumni Association of the Mayo Foundation; a corresponding member of the Scandinavian Orthopedic Society; fellow of the American College of Surgeons; in 1954 received a certificate of merit from the American Medical Association for an exhibit on Primary Tumors of the Soft Tissues of the Extremities Exclusive of Epithelial Tumors—An Analysis of 500 Consecutive Cases and in 1956 received a certificate of merit for exhibit on Bone Tumors; served on the staffs of the St. Mary's and Colonial hospitals in Rochester, Minn.; a consultant in his specialty to the U. S. Veterans Administration; served as a member of the advisory committee of the Children's Bureau of the U. S. Department of Labor; in 1942 gave the William J. Mayo Clinic Lecture at the University of Michigan in Ann Arbor; in 1957 was honored by former fellows in orthopedic surgery of the Mayo Foundation and colleagues at the Mayo Clinic with the establishment of the Ralph K. Ghormley Traveling Scholarship; joint author of "Diagnosis in Joint Disease: a Clinical and Pathologic Study of Arthritis"; editor of a volume "Orthopedic Surgery" published in 1938; associated with Monterey (Calif.) Hospital and the Peninsula Community Hospital, where he died June 6, aged 66.

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Philp-Bradshaw, Martha, San Francisco; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1902; for many years a medical missionary in China; died May 29, aged 89.

Powell, Eppie Clifton, Middlesex, N. C.; University of Nashville (Tenn.) Medical Department, 1907; chairman of the Nash County Board of Health and Middlesex School Board; for many years physician to the Free Will Baptist Orphanage; a director of Peoples Bank & Trust Company; past-president of the Middlesex Rotary Club; died in the Wayne Memorial Hospital, Goldsboro, May 26, aged 75.

Ray, Fred Merton Ⓜ Pocatello, Idaho; Northwestern University Medical School, Chicago, 1909; veteran of World War I; associated with St. Anthony Hospital and Bannock Memorial Hospital, where he died May 29, aged 77.

Roark, Jesse Lawrence, Albuquerque, N. M.; born in Water Valley, Miss., Sept. 30, 1895; Jefferson Medical College of Philadelphia, 1924; served overseas during World War I; interned at the Jefferson Medical College Hospital in Philadelphia and served a residency at the White Haven Sanitorium in White Haven, Pa.; at one time on the teaching staff of his alma mater; formerly medical director of Lafayette and Yalobusha counties in Mississippi; served on the staffs of the Mississippi State Sanatorium for Tuberculosis in Sanatorium, Pennsylvania State Sanatorium for Tuberculosis in South Mountain, Pa., Essex County Sanatorium for Tubercular Diseases in Verona, N. J., and the Arkansas

Tuberculosis Sanatorium in State Sanatorium; died in the Veterans Administration Hospital May 31, aged 63.

Roth, Charles Rudolph Ⓜ Chicago; Northwestern University Medical School, Chicago, 1906; associated with the Illinois Masonic Hospital; died June 8, aged 82.

Russell, Grover Cleveland Ⓜ Jackson, Miss; Medical Department of Tulane University of Louisiana, New Orleans, 1909; at one time practiced in Johns, serving as health officer of Rankin County for many years; associated with the Mississippi Baptist Hospital; died June 8, aged 74.

Russell, Marion Fore Ⓜ Great Bend, Kan.; born in Alma, Va., Aug. 23, 1884; University of Pennsylvania Department of Medicine, Philadelphia, 1907; past-president of the Barton County Medical Society; fellow of the American College of Surgeons and president of the Kansas Chapter; served as county coroner; for many years associated with the Boy Scout movement and in 1943 was honored with the Silver Beaver Boy Scout award; member of the staff of St. Rose Hospital, where he was chief of staff from 1937 to 1945; past-president of the Great Bend Rotary Club; a director of the American State Bank; vice-president and a director of the Prudential Building & Loan Association; died May 31, aged 74.

Sanford, Benjamin Bentley Ⓜ Portland, Maine; Tufts College Medical School, Boston, 1924; veteran of World War II; served as a colonel in the U. S. Air Force Reserve; died May 25, aged 59.

Stadulis, Ignatius Martin, Wilkes-Barre, Pa.; Jefferson Medical College of Philadelphia, 1924; veteran of World War I; medical inspector for Hanover Township schools for many years; on the staff of the Mercy Hospital; died June 1, aged 60.

Stanley, Thomas Eldridge Ⓜ Richmond, Va.; Medical College of Virginia, Richmond, 1932; interned at the Hospital of St. Vincent de Paul; served as chairman of the school board of Hanover County; a staff member of St. Elizabeth's Hospital, where he died June 3, aged 50.

Stewart, James Leon, New York City; Université de Lyon Faculté de Médecine et de Pharmacie, France, 1919; associated with the French Hospital, where he died April 19, aged 67.

Schnitzler, Friedrich Wilhelm Ⓜ Woodmere, N. Y.; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1921; died May 22, aged 69.

Stone, William Ernest Ⓜ Boonville, Mo.; Washington University School of Medicine, St. Louis, 1918; veteran of World Wars I and II; past-president of the Cooper County Medical Society; past-chief of staff at St. Joseph Hospital; died in the Veterans Administration Hospital, Wadsworth, Kan., May 14, aged 67.

Tinsman, Eugene, Orient, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1903; served on the school board for many years; member of the medical examining board for the World War II draft and received a citation signed by President Franklin D. Roosevelt and a selective service medal from Congress; died May 24, aged 85.

Watson, Cassius Hinds Ⓜ Brookfield Center, Conn.; Long Island College Hospital, Brooklyn, 1905; served on the faculty of his alma mater; medical director of the American Telephone and Telegraph Company from 1915 to Oct. 1, 1943, when he retired; past-president of the National Safety Council and the American Association of Industrial Physicians and Surgeons; fellow of the American College of Surgeons; formerly associated with the Bushwick and Eastern District hospitals in Brooklyn; past-president of the Stony Wold Sanatorium in Lake Kushaqua, N. Y.; died in Stamford, June 1, aged 80.

Webster, Hugh Martin Jr., Huntsville, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1950; veteran of World War II; died May 30, aged 32.

Wellman, Graham Ormond, Carthage, Mo.; Hahnemann Medical College and Hospital of Philadelphia, 1913; served in France during World War I; died May 28, aged 76.

Williams, Tom Alfred, London, England; University of Edinburgh Faculty of Medicine, Edinburgh, Scotland, 1896; for many years practiced in Washington, D. C.; past-president of the Washington Psychological Society and the Washington Society of Nervous and Mental Diseases; died in Bournemouth, England, May 27, aged 89.

Yale, Arthur Wells, San Diego, Calif.; Hahnemann Medical College and Hospital of Philadelphia, 1899; veteran of World War I; died in Bellflower May 23, aged 83.

Zeller, Raymond Bryant Ⓜ Hazlehurst, Miss.; Jefferson Medical College of Philadelphia, 1927; member of the American Academy of General Practice, American Association for the Advancement of Science, and the American Association of Railway Surgeons; for many years secretary of the Tri-County Medical Society; veteran of World War I; past-vice-president of the Jefferson Medical College Alumni Association; past-president of the staff, Hardy Wilson Memorial Hospital; died June 4, aged 58.

FOREIGN LETTERS

BRAZIL

Intestinal Schistosomiasis.—Many surveys carried out in different areas have demonstrated that schistosomiasis, imported from Africa with Negro slaves and neglected for decades, now affects about 4 million persons in Brazil, mainly in the northern tropical section. Federal and state control programs are now yielding appreciable results. At a meeting of the Rio de Janeiro Medical and Surgical Society Dr. Mario Pinotti, Minister of Health, said that in infected districts of seven states the disease is being combated intensively with several methods of attack; in 8 others, where the problem is less severe, only partial measures are being used; and in the remaining states and territories schistosomiasis has not been reported.

The control measures include the use of such chemical molluscacides as copper sulfate and sodium pentachlorophenate. Three or four times a year snail-infested waters are treated with 1 Gm. of the latter per 100 liters. Sanitary engineers are also building water purification systems in rural communities and constructing bath houses and communal laundries with clean water supplies. Unsanitary lakes and streams are being placarded with warning posters. Another measure adopted to combat the disease is the mass treatment of infected persons, with tartar emetic, emetine, stibophen, lucanthone, and other drugs. Free treatment centers were installed by the Ministry of Health. Twenty-seven communities were freed from the disease in 1958, but they must be protected by a strict control of internal migrations of the population.

Gallstone Ileus.—J. von Sonnleithner, of Sanatório São Lucas in São Paulo, operated on a patient with gallstone ileus in whom a large migrating calculus stopped in the first part of the jejunum. This was the 26th such case reported in Brazil. Last year, Helio Silva (*Bulletin of the Brazilian College of Surgeons*) collected a series of 500 such cases from the world literature. In this series the sex ratio was one man to seven women. Most of the patients were over 50 years of age.

Complications After Pulmonary Resection.—Although adequate preoperative treatment and more precise indications in pulmonary resections have markedly lowered the incidence of postoperative complications, such complications after resections for treatment of tuberculosis are still rather frequent. C. Frazzato Jr. and co-workers of the São Paulo Hospital (*Rev. paulista med.* 54:253, 1959) treated 31 patients with pulmonary tuberculosis who had had adequate medical treatment for at least one year. During the preoperative preparation of the patients treatment with isoniazid and streptomycin was continued. In two of four patients given penicillin and streptomycin by inhalation a remission occurred. The remaining patients were operated on. Para-aminosalicylic acid was not used in the preoperative preparation, although some patients had received this drug in previous ambulatory treatment.

The basic indication for resection was a residual lesion after adequate treatment, with or without positive sputum. All patients had obligatory indications for operation: 13 had a cavity in an upper lobe; 6 a cavity in the middle or a lower lobe; 6 fibrosis, atelectasis, and bronchiectasis; one an extensive unilateral lesion and residual lesion after thoracoplasty; and one a tuberculoma of the base of the right lung. Thirty-two resections (10 pneumectomies, 17 lobectomies, and 5 lobectomies with segmentary resections) were performed in the 31 patients. The cavities of all patients were drained under water, since this is a routine procedure at that hospital, where drainage is considered useful postoperatively. Other postoperative measures included antibiotic treatment, sedation (without morphine), early ambulation, fluids by mouth, and specific antituberculosis treatment.

The authors observed 54 complications (not counting 2 of a general surgical nature): residual sack in 10, suppuration in 9, fistula in 8, empyema in 8, shock in 4, hemothorax and pleural hemorrhage in 3, atelectasis and secretions in 2, reactivation in 2, cardiac insufficiency in 2, subcutaneous emphysema in 2, respiratory insufficiency in 2, and total dehiscence in 2. Such complications occurred in 22 patients, but in 6 the complications were so mild (e. g., small effusion or scanty suppuration) that these patients can be grouped with the remaining 9, thus making a total of 15 patients with results considered excellent. Six patients were cured after complications, two continued to have sputum positive for tubercle bacilli, and eight died. The length of postoperative hospitalization was markedly increased by the complications. Fistulas were the most serious complications. Pneumectomy revealed itself as a major surgical risk, since 6 of the 10 patients on whom it was performed died. Serious complications always followed this type of operation and were usually fatal.

The items in these letters are contributed by regular correspondents in the various foreign countries.

The anesthetist has an important role in meeting the problems of secretion. The endobronchial intubations and the tamponment of the drainage bronchus must be the rule in pulmonary resections. Besides preventing internal drowning they permit a better surgical technique. Adequate chemotherapeutic and antibiotic treatments of tuberculosis in the preoperative and postoperative periods not only diminish the incidence of complications but also permit more boldness in the operative indications. Thus, patients with severe infections, cavitation, and even empyema with bronchial fistula can be operated on with success.

Blastomycosis.—J. Machado Jr. and J. L. Miranda (*O Hospital,* May, 1959), reported an epidemiologic study of South American blastomycosis. Between November, 1949, and January, 1959, they studied a series of 238 patients. Those most severely affected were in the 40-to-49-year-old group. There was no indication of frequency related to race. Women were less affected than men, but this was probably due to occupational factors. The infection was most common in farmers. The portals of entry of the parasite were the skin and the mucosa of the respiratory and digestive tracts, especially the oral muscosa.

Paranasal Tumors.—J. F. Barbosa, chief surgeon of the head and neck department of Central Institute of Cancer in São Paulo, analyzed a series of 141 patients with malignant tumors of the paranasal cavities. Of these 116 were Caucasian, 21 Negro, and 4 Oriental; 97 were men and 44 were women. Most of the patients were between the ages of 40 and 70 years. The author treated such patients by removing the upper portion of the ascending branch of the mandible, the lower portion of the temporal muscle, the upper portion of the masseter, the zygomatic arch, and all of the external pterygoid muscle. He exposed, tied, and severed the internal maxillary artery before removing the tumor. All the contents of the orbital cavity and the ethmoid sinus were included in the resected mass. As a rule, he covered the operative cavity with a free flap. The results of this treatment were encouraging.

Pancreatic Cysts.—Although pancreatic cysts are rare, four cases were presented by J. R. Alves, professor at the University of Minas Gerais, in Belo Horizonte. Two were true cysts and two were pseudocysts. In all the patients the diagnosis of pancreatic cyst was made preoperatively. In one there was a concomitant disease of the extrahepatic bile passages. In one there was a simultaneous occurrence of diabetes and trypanosomiasis. One case was probably due to a chronic pancreatitis with pancreatic fibrosis. There is no standardized operation for all cases. Splenectomy was necessary in two cases, owing to the extensive adhesions between the cyst and the spleen. All the patients recovered and returned to their normal activities.

DENMARK

Peptic Ulcers due to Corticosteroids.—A series of 10 patients who had peptic ulcers that developed during long-term steroid therapy with relatively small doses was reported by Aagaard and co-workers (*Acta chir. scandinav.* 116:423-428, 1958-1959). The ulcer involved the stomach in seven, the pylorus in two, and the jejunum in one. All 10 patients were operated on and had no postoperative complications. These ulcers were similar to ordinary gastric ulcers, apart from a less dramatic course during perforation. The steroids have two effects that might be assumed to be important in the development of peptic ulcers; they increase the production of hydrochloric acid and pepsin, and they inhibit fibroblast proliferation during wound healing and delay the formation of granulation tissue.

Types of Honors.—When one has reached the age of 70, or thereabouts, and has had a distinguished career, one's admirers may wish to express their appreciation by a collection containing original articles—many perhaps of great value. When such a volume is published by itself and not as a part of, or supplement to, a well-established medical journal, it often escapes the notice of librarians and others engaged in indexing and cataloging medical literature. The smallness of the mailing lists of some collections of this sort may contribute to the burial of their contents. To escape this fate B. Ibsen (*Nordisk medicin,* April 23, 1959) presented some alternatives. If the collection is to survive as such, it must be published in a medical journal with a substantial mailing list. If such a literary testimonial is not contemplated, the prospective contributors might find a channel for their emotions in the establishment of a prize to be given in the name of their idol. The award, from time to time, of this prize to some worthy recipient would remind the world of its debt. On the other hand, a fund collected in honor of the distinguished scientist might be earmarked for the remuneration of lecturers on given subjects. The author's pet idea, however, was to send the beloved septuagenarian on a journey to enlighten others by giving lectures himself.

Rehabilitation of the Nervous Patient.—K. H. Backer has published, through the University of Copenhagen, a monograph in which he reviews, from the point of view of rehabilitation, the fate of the patients discharged from the surgical and medical wards of a large Danish hospital in 1949. The rehabilitation movement at first stressed such dramatic ailments as paralysis, spasticity, blindness, deafness, and crippling. These tended to overshadow the less striking mental handicaps, which, in the form of mild neurosis, psychopathy, or just slight mental deficiency, have interfered with wage-earning and a congenial mode of life. The author makes an urgent plea on behalf of the latter group.

Two 50-Year Jubilees.—In 1909 the National Health Service (NHS) and the Medical Jurisprudence Council came into being. Both have earned the general esteem they now enjoy by the skill with which their leaders have made them indispensable to the community. The present head of the former body, J. Frandsen (*Ugeskrift for laeger*, April 23, 1959), states that his predecessors had to fight in order to fit adequately into the machinery of a modern welfare state. With responsibilities to such important activities as dentistry, nursing, and pharmacy, to mention only three of the many spheres in which the NHS is interested, it acts in rather an advisory than a disciplinary capacity, not being a ministry of health nor the health department of some ministry or other. It is an autonomous institution, beyond the bounds of a central administration although connected with it and with local administrations. So long as the health activities of the country are decentralized, the NHS can successfully meet the calls made on it.

In *Ugeskrift for laeger* for April 30, Prof. K. Sand, head of the Medical Jurisprudence Council for over 30 years, traced its history since its birth in 1909. Here, too, is a record of prodigious growth from modest beginnings. With the growth of a third powerful organization, the Danish Medical Association, which works in close cooperation with the NHS, Denmark has built up a system of public health which may well serve as a model for other countries.

Pertussis Vaccination.—At the state serum institute in Copenhagen tests have been made for some time with a triple vaccine against diphtheria, tetanus, and pertussis, with a view to observing the severity and frequency of its side-effects. While awaiting a final verdict attention is being focused on pertussis vaccine alone, as given to prevent whooping cough early in infancy. As pointed out by H. Lautrop and co-workers (*Ugeskrift for laeger*, May 21, 1959) whooping cough continues to take a heavy toll of life in Denmark, with an average of about 25 deaths a year. About 75% of these occur in children under 1 year of age. There is also an unknown number of cases of bronchiectasis and other sequels to whooping cough that are not immediately fatal, hence the advice to start vaccination against it as early as the 5th week of life. Two further injections should then be given at intervals of a month, to be followed about a year later by a fourth injection. In the absence of such prophylactic vaccination it may be permissible to fall back on therapeutic injections just before or at the outbreak of whooping cough, but no extravagant claims can be made for such action.

Addiction to Tranquilizers.—J. Schou (*Ugeskrift for laeger*, April 23, 1959) stated that in 1958 over 24 million grams (61 million 400-mg. tablets) of meprobamate was sold. It is so popular with would-be suicides that 33 cases have already been reported in which it was the sole agent, in amounts varying from 8 to 40 Gm., in an attempt to commit suicide. None of these attempts proved fatal. In another series of attempted suicides in which meprobamate was given with a barbiturate there were two deaths. Although there were no deaths in the first series, the author warned against a too light-hearted prognosis, as only 6 Gm. given by mouth may induce a dangerous comatose intoxication. The risk of meprobamate addiction is now regarded as being so serious in Denmark that the author warned against its use for the cure of tobacco addiction.

Thallium Poisoning.—A discussion at a recent meeting of the Danish Society for Internal Medicine (*Nordisk medicin*, May 21, 1959) showed how polymorphous the manifestations of poisoning with thallium may be, whether it is taken in an attempt to commit suicide or by accident. In one series of six cases there were five in which thallium destined for rats and mice had been taken by mistake. Alopecia has been said to be a sure sequel to thallium poisoning, but it was observed in only two of these cases. The diagnosis of thallium poisoning may be comparatively easy when the characteristic alopecia appears several days after the poison has been taken, but it is less so when the clinical findings are suggestive of poliomyelitis. One of the patients in the above-mentioned series underwent a laparotomy, since violent colic had seemed to indicate thrombosis of some mesenteric vessel. One speaker at this meeting stressed the diagnostic value of tests of the urine for thallium, which in one of his patients was found in such quantities as to indicate that a lethal dose had been taken. As a result of prompt action the patient recovered, however.

FINLAND

Postoperative Biliary Stones.—Operations for biliary stones are sometimes complicated by concrements retained in the biliary ducts. A conservative method for the removal of such concrements is based on the lipid-dissolving property of ethyl ether. The chief reasons for the retention of stones in the biliary ducts are that they are situated high in the hepatic ducts, whence they may later migrate with the bile flow down into the common bile duct; or that by the action of inflammatory processes the stones may become imbedded in the wall of the common bile duct or hidden in a cystlike cavity near the duodenal papilla, thus escaping observation; or, finally, that obesity or impaired general condition may limit the surgical possibilities and render operative cholangiography difficult. Alfthan and Köhler (*Acta chir. scandinav.* 116:437-449, 1958-1959) reported on 24 patients aged 27 to 68 years, in whom postoperative residual biliary tree stones were found. These patients represented 1.4% of all who had had operations for gallstones performed in the period 1954-1958. Of the 24 patients 14 were relieved of stones. From a clinical point of view ethyl ether seemed to be the best of all lipid solvents. Chemical analysis or, at any rate, a dissolving test in vitro before treatment, was recommended.

In the beginning the treatment should be cautious. Either the initial doses of ether should be small (about 0.5 ml.) or the ether should be given through a double-barreled tube, allowing the vapor to escape when the pressure rises. The authors did not observe any harmful side-effects of the ether. Concrements larger than 1 cm. in diameter can seldom be dissolved, and therefore comparatively early reoperation for such stones is indicated. Intrahepatic stones dissolve slowly and demand persistence. Small, common-duct stones generally dissolve within two to three weeks. A single dose of ether remains in the biliary ducts for about 10 minutes. The authors therefore recommended frequent treatments, prolonging the action of the ether as much as possible each time. Operative cholangiographies of a high technical standard probably afford the best possibility of visualizing stones in the biliary tree and should be made, if possible. If, however, stones persist in the biliary ducts, the authors recommend ether treatment first. Only if this procedure failed should reoperation be performed.

INDIA

Induced Cardiac Arrest.—A. K. Basu and co-workers (*Indian Journal of Surgery*, vol. 21, April 1, 1959) induced cardiac arrest in adult monkeys by using two salts of potassium citrate: potassium chloride and acetylcholine. The experiments were done in both hypothermic and normothermic animals, after anesthesia was induced with an intravenous dose of thiopental and intratracheal intubation. Cooling was done by immersion and by rubbing ice on the hide, the range of hypothermia varying from 29 to 30 C (84 to 86 F). Cardiac arrest with acetylcholine occurred within a few seconds of administration of the drug. The myocardium retained a certain amount of tone and was not completely flaccid during the arrest. The revival of cardiac rhythm and contraction was easier and more spontaneous than when potassium salts were used. The incidence of fibrillation was less with acetylcholine, and, even if it did occur, it could be easily controlled. An injection of atropine served as an effective antidote, causing a smooth and quick reversion.

The disadvantage of acetylcholine was that the arrest it produced was temporary and often incomplete. This was seen in both hypothermic and normothermic animals. Even as large a dose as 300 mg. did not produce total arrest. The recovery in normothermic animals was even smoother than in hypothermic animals. Fibrillation did not occur in any of these animals. Thus, hypothermia did not offer any added advantage but on the contrary caused minor periods of fibrillation in the recovery phase. The dose of potassium salts varied from 75 to 300 mg., depending on the weight of the animal. The asystole induced by these salts was completely flaccid and absolute, the duration varying from 5 to 19 minutes. Some animals, however, had a definite but variable latent period between the injection and the arrest. Cardiac dilatation and ventricular fibrillation occurred in almost all animals during recovery. The duration and severity of these fibrillatory episodes was much more marked than after acetylcholine, and there was no certain way of terminating them as there was when acetylcholine was used.

Potassium-induced arrest was considered to be of greater help in open cardiac surgery than that induced by acetylcholine, because of the complete flaccidity of the myocardium and the longer duration of the asystole. Its disadvantages were the constant occurrence of cardiac dilatation on releasing inflow occlusion and the development of severe ventricular fibrillation before the return to sinus rhythm. Manual cardiac massage was found useful for treating fibrillation, but it had to be continued for a long time (19 minutes in some animals) before normal rhythm was reestablished. Calcium chloride injection was of doubtful value in treating fibrillation, and coronary infusion of sodium lactate solution was of no value. Hypothermia was of great help in potassium-induced arrest. Of the 11 animals on whom hypothermia was used 8 survived, while survival was rare in the normothermic controls. No brain damage could be detected in the hypothermic animals in whom fibrillation lasted for more than 15 minutes and in whom normal rhythm was ultimately reestablished by massage.

In the same issue P. K. Sen and co-workers reported a study on healthy mongrel dogs in which they assessed the action of different cardioplegic agents, alone and in combination. Anesthesia was induced with intravenous administration of thiopental sodium, and positive-pressure ventilation with air by a respiratory pump through an endotracheal tube was used from the start. Inflow occlusion was practiced on all animals before bringing about chemical cardiac arrest. The cardioplegic drug was injected into the ascending part of the aorta till the heart stopped in diastole. After allowing a certain interval, depending on the type of arrest, various substances were used to wash out the cardioplegic drug, such as whole blood, Ringer's solution, 5% dextrose solution, normal saline solution, and 10% sodium lactate solution. In many animals injections of calcium and epinephrine and cardiac massage had to be resorted to for restitution of heartbeats to normal rhythm. Hypothermia was produced by immersion in an ice-cold water bath when required, the hypothermia being only of moderate depth (about 28 C [82.4 F]).

The various chemical agents tested were potassium citrate alone, acetylcholine alone, combination of potassium citrate and acetylcholine, potassium citrate and acetylcholine under hypothermia, potassium chloride and acetylcholine under hypothermia, and a combination of magnesium sulfate, potassium citrate, and prostigmine. Nine dogs received potassium citrate alone, a 25% solution being used for the first dog, a 10% solution for the next, and a 5% solution for the rest, its amount varying from 250 to 1,250 mg. All the hearts went into ventricular fibrillation during recovery after a diastolic arrest of one to four minutes. Manual cardiac compression and injections of calcium chloride, epinephrine, and occasionally neostigmine were necessary for restitution. Another group of nine dogs received acetylcholine alone. Diastolic arrest occurred within a few seconds but lasted less than a minute. Normal rhythm was restored in all but one who developed ventricular fibrillation. There was no evidence of brain damage in the dogs that survived, the longest survival time being eight days.

Five dogs were injected with acetylcholine and potassium citrate, the former in the same dose as in the second group and the latter in 1% solution in amounts varying from 60 to 100 mg. Diastolic arrest occurred rapidly in all and restitution was started after an interval of two to five minutes. Four animals came back to normal with massage alone, and one required an injection of calcium chloride. Ventricular fibrillation developed in all animals during this process, and it remained permanent in one. The time required for restitution ranged between 4 and 20 minutes and all showed evidence of brain damage. Thirteen animals received the same combination as had the previous group under hypothermia ranging between 30 and 32 C. Diastolic arrest was immediate and was maintained for two to seven minutes. Three animals required intracoronary calcium chloride injection besides massage for restitution, the time required for restitution varying between ½ minute and 20 minutes. Brain damage was definite in two and possible in two others. There were no long-term survivals.

Ten dogs received a combination of 1.2% potassium chloride solution and 2% acetylcholine solution under hypothermia of 30 C. Diastolic arrest was obtained in all within one to four minutes. Six dogs were revived with cardiac massage of one to seven minutes' duration and the remaining four did not respond to either massage or an injection of calcium chloride. Seven developed ventricular fibrillation during restitution. Ten animals were treated with a mixture of magnesium sulfate, potassium citrate, and prostigmine, after induction of hypothermia of 30 C. Diastolic arrest was maintained for two to four minutes in all, but the arrest occurred after a latent period of one-half to two minutes after injection. Seven animals were restored to normal by massage, and some also required an injection of calcium chloride. The time necessary for restitution varied between 2 and 23 minutes. Ventricular fibrillation occurred in only three dogs, one of which was restored to normal after 23 minutes of cardiac massage and an intracoronary injection of calcium chloride. The other two could not be revived.

Thus, of all the agents used, acetylcholine had the most rapid action but the arrest was incomplete and of short duration. Potassium-induced arrest was rapid and complete but recovery was uncertain, often late, and accompanied by ventricular fibrillation. A combination of these two exhibited the balanced action of rapid diastolic arrest of relatively shorter duration but an easier restitution of rhythm. The incidence of ventricular fibrillation was, however, as frequent as with potassium alone. A mixture of magnesium sulfate, potassium citrate, and prostigmine produced a slower but definitive diastolic arrest with the least incidence of ventricular fibrillation and a reversible cardiac standstill.

JAPAN

Artificial Insemination.—According to the *Tokyo Weekly* (May 31, 1959) the Department of Family Planning of Keio University School of Medicine celebrated the 10th anniversary of its successful artificial insemination program. The first child resulting from artificial insemination in Japan, a girl, is in the fifth grade and is bright and pretty. In the past 10 years 300 babies were conceived by this method. Understandably the mothers prefer to remain anonymous. Because of this the director of the department is handicapped in carrying out a complete follow-up study. More than 50% of the mothers ignore questionnaires. After becoming pregnant many mothers prefer to be delivered elsewhere and are lost to the study. In many cases two or three inseminations are required before pregnancy occurs. If after 6 attempts conception does not take place the would-be mothers receive no further encouragement.

The candidates are first referred to the gynecologic department for a potency test, biopsy of the endometrium, and culture of menstrual discharge for tubercle bacilli. If these tests reveal no abnormality, a sample of the husband's semen is examined. If this is found to be deficient in any way both parties are asked to sign a document, separately, giving unqualified consent to the use of the stock sperms. Ovulation is presumed to coincide with the elevation in body temperature of the prospective mother, who is instructed to visit the clinic on the day of presumed ovulation. Reasons given for requesting artificial insemination included the fact that (1) the husband worked in an atomic energy plant and the couple feared damage to his sperms, (2) husband and wife were related and they feared passing on a hereditary disease, and (3) husband and wife were separated but the wife still desired a child of her own. The sperm stocks used were procured from medical students or athletes who received a small fee. Controversies arising from various aspects of this subject have not yet been resolved.

UNITED KINGDOM

Ultrasonic Vibrations.—Because of the danger of exposing the fetus to x-rays, tests are being carried out in the department of obstetrics of Glasgow University to ascertain if the fetal and maternal abnormalities that are detected radiologically at present may be determined by ultrasonic vibrations instead. In most hospitals the number of radiologic examinations during pregnancy is being reduced to a minimum because of the hazards of irradiation to the fetus. Two physicists have been appointed to the Western Regional Hospital Board in Scotland and funds allocated to study the diagnostic uses of ultrasonic vibrations such as have already been used for the diagnosis of abdominal tumors.

Culture of Sarcoid Tissue.—Lundbek and co-workers reported the successful culture of sarcoid tissue from lymph nodes and skin by means of the plasma-clot technique (*Brit. J. Exper. Path.* 40:61, 1959). Lymph nodes from the supraclavicular fossae or skin sarcoids were removed under local anesthesia and cultured in plasma-clot or bovine amniotic fluid enriched with horse serum and bovine or human embryonic extract. Within a few days the tissue fragments were surrounded by a carpet of fibroblasts, which became swollen and enlarged, their chromatin became coarse, and the cells gradually rounded off. These changes were patchy. In nearly all of these patches a number of giant cells developed. Most of the cells contained large eosinophilic cytoplasmic inclusions. These changes were not seen in lymph nodes and skin removed from patients with other conditions associated with lymphadenopathy, such as Hodgkin's disease. The cytoplasmic inclusions could have resulted from the activity of an infectious agent, although this was not proved. Tests are being made to see if these inclusions can be maintained by passage. Attempts to establish transferable cytopathogenic effects with sarcoid lymph nodes and skin in human embryonic lung tissue cultures failed.

Cost of Drugs.—According to the final report of the Hinchliffe Committee the drug bill in relation to the total cost of the National Health Service (NHS) in England and Wales has doubled in the last nine years, despite efforts to curb it. Making allowance for the fall in the value of money, this represents a real increase of about 45% since the fiscal year 1949-1950. While there is no evidence of widespread and irresponsible extravagance in general practitioners' prescribing, there is room for economy. The tendency to order larger quantities of each prescription than are required involved some waste. The cost of the average prescription has risen from 43 to 84 cents, and the average cost of drugs per patient a year has risen from $2.27 to $4.20. No explanation was found for the continuing per capita rise in prescriptions in a period when the improved efficacy of drugs should have shortened the length of illness and returned people to health and work sooner.

The committee recommended that physicians be given more information on prescribing, especially about the costs and advantages and disadvantages of new drugs. They should not prescribe expensive preparations when simpler, equally effective, preparations are available. There should be no ban on the prescribing of new drugs but, until the results of clinical trials are known, doctors should prescribe new drugs only when existing ones have failed. If a given doctor's costs habitually exceed the local average by more than 50% the reason should be sought by the local medical committee. The penalties for excessive prescribing, particularly if a physician prescribes extravagantly to attract patients, should be severe. Some patients exert pressure on their doctors to prescribe particular drugs for them. Posters and notices should be supplied for offices warning patients against "getting the medicine habit."

All medical schools should be encouraged to take an interest in economy in prescribing. More students should spend short periods with general practitioners. There is an urgent need for systematic postgraduate instruction of general practitioners in pharmacology and therapeutics. Every consultant should exercise a proper economy in his own prescribing for hospital patients. Everything possible should be done to prevent public money from being wasted in inflated and expensive sales promotion. The drug industry should be asked to curb the more extreme forms of advertising. New drugs should be subjected to independent controlled clinical trials as early as possible with speedy publication of the results. One of the committee's chief recommendations was that an advisory body including men with business experience, an economist, and a statistician, be appointed to advise the Minister of Health at an early date on matters affecting drug costs.

Referring to new drugs, the committee said that 18% of all NHS prescriptions in 1950 were for proprietary drugs. This proportion rose in 1957 to just under 50%. In the same period the value of proprietary drugs rose from about 40 to over 67% of the total cost of prescriptions, measured by the cost of ingredients. A recent estimate showed that two groups of drugs, antibiotics and hormones, were together responsible for almost 35% of the total ingredient cost of proprietary preparations.

Doctors Urged to Unite.—British Medical Association leaders urged the 40,000 National Health Service doctors to unite in readiness for a dispute with the government over the report of the Royal Commission on Doctors' and Dentists' Remuneration and any action necessary to back their pay claim. The policy of the 21,000 family physicians was laid down at the annual conference of representatives of local medical committees in London in June. The General Medical Service Committee, which negotiates for family doctors, said: "Under extreme provocation the profession should reserve the right to withdraw from the service." The committee will recommend a total withdrawal of service, with a return to private practice, in the event of an unresolved dispute with the government, but, it warns, that such action would be possible only if the profession was united and resolved to make a stand on principles rather than on matters of remuneration alone.

Hypertension.—A. W. D. Leishman of the United Sheffield Hospital (*British Medical Journal*, May 30, 1959) has followed the progress of 211 untreated hypertensive patients regularly since 1946 and compared it with that of 73 patients treated by lumbodorsal sympathectomy and 118 treated with ganglion-blocking drugs. Half of the untreated patients are dead, and a study of these cases has confirmed that high diastolic pressure, male sex, and the presence of albuminuria or retinopathy are particularly unfavorable features. Changes evident in the electrocardiogram did not appear to influence the prognosis. Rise of blood pressure in untreated patients was uncommon, but in 20 of 176 patients the diastolic pressure increased by 20 mm. Hg. Seven of these developed malignant or accelerated hypertension. This could not have been foreseen when they were first examined. A satisfactory fall in blood pressure was achieved in 80% of the patients who underwent lumbodorsal sympathectomy. The unusual permanence of these results was attributed to extensive dorsal denervation. Ganglion-blocking drugs were given parenterally. Of the patients at present on treatment, 67% were regarded as well controlled.

The treated and untreated groups were judged to have been of equal severity, and comparison of their respective mortality rates was made. Except in malignant hypertension the death rate among treated patients was in no instance appreciably higher than one-third that of the untreated group. Although the length of observation of drug-treated patients was not yet adequate for strict comparison, these figures left no doubt that lives had been extended by both forms of hypotensive treatment. Reduction in the number of fatal strokes was a notable feature. Judged from the fate of untreated patients, the use of ganglion-blocking drugs seemed justified in any person whose diastolic pressure was consistently above 120 mm. Hg, and in the presence of albuminuria it might be advisable when blood pressure was below this level. Hypertensive women, however, did not normally require this treatment unless the diastolic pressure was at least 130 mm. Hg.

M. J. D. Newman and J. I. S. Robertson of St. Mary's Hospital, London, reported in the same issue that they made a survey of 104 patients with initial diastolic pressures over 120 mm. Hg. Most of these patients were treated with ganglion-blocking drugs. The complications occurring were related to the degree of control of the diastolic pressure. In patients with retinal hemorrhages and exudates or papilledema the prognosis was closely related to the degree of lowering of the blood pressure. In those patients with cerebral or cardiac vascular lesions no such relationship could be clearly discerned. Uncomplicated hypertension has a comparatively good prognosis without treatment, and a much larger series would be required to demonstrate any effect of hypotensive drugs.

Cancer Research.—In the British House of Commons, Mr. Sydney Irving asked how much money would be spent by the Minister of Health on cancer research this year. The minister replied that expenditure from public funds on cancer research was mainly undertaken by the Medical Research Council, which expected to spend $1,624,000 for this purpose during the current year, including a grant of $578,000 to the Institute of Cancer Research. Cancer research is also carried out in the National Health Service in the course of treating patients, but it was impossible to make a separate estimate for the expenditure involved. Mr. Irving had nothing but praise for the effort made by voluntary agencies, but he found it hard to understand why, in the attack on this terrible disease, so much of the burden should fall on voluntary effort.

Redundant Consultants.—An annotation in the *British Medical Journal* of June 6 said, with reference to the reinstatement of a dismissed consultant, that the way is now open for belated justice to be accorded to Mr. A. H. Barber, the Oldham gynecologist whom the Manchester Regional Hospital Board wrongfully dismissed in 1952. The Minister of Health has amended the National Health Service Regulations so that now regional boards may offer employment to redundant consultants without creating competition. The new regulations became effective May 27 and apply to Scotland, England, and Wales. After a seven-year battle, which included a successful high court action, repeated pressure on the Ministry by the British Medical Association (BMA) and the Joint Consultants Committee, a campaign in the lay press, and questions in both Houses of Parliament, bureaucratic rigidity and inertia are exposed. It now remains for the Manchester board swiftly to find suitable work for Mr. Barber.

The new regulations go much further than making justice for one man administratively possible. Clause 16 of the Terms and Conditions of Service of Hospital Medical Staff is the only safeguard for consultants against unfair dismissal. It is written into their contracts with regional boards. For a long time the BMA and the Joint Consultants Committee have been imploring successive ministers of health to give substance to their paternal assurances and certainty to their understanding of moral obligation. The new regulations appear to do this. "When as a result of contraction of work or of local reorganization," states the Ministry's explanatory memorandum to hospital authorities, "it becomes, or has become, necessary for a board to terminate the appointment of a consultant or a senior hospital medical or dental officer, the board should first consider whether they can vary his contract and offer him alternative employment. An appointment offered in these circumstances need not necessarily be in the same specialty as the officer's existing post, provided that he has the necessary qualifications for the new post." If the board has no post to offer, and the officer assents, the board should notify all other boards. This is a step toward remedying a serious defect in the terms of employment in the hospital service.

Mammary Cancer.—For many years radical mastectomy, either alone or in combination with radiation therapy, was generally considered the best treatment for operable cases of breast cancer. This, however, has been challenged by McWhirter, of Edinburgh, who advocated simple mastectomy, followed by postoperative irradiation of the axilla, supraclavicular glands, and chest wall for all but advanced cases. Watson has compared the gross five-year survival rates of patients treated by the two methods (*Lancet* 1:1191, 1959). McWhirter's five-year survival rate for 1,882 patients at Edinburgh Royal Infirmary, treated when feasible by simple mastectomy and postoperative irradiation, was 42%. Watson's figures were obtained from the Saskatchewan Cancer Treatment Service, which operates under the auspices of the Canadian government. In the Saskatchewan series 1,055 patients were treated by radical mastectomy and in most this was followed by irradiation. The gross five-year survival rate was 52%. The difference is statistically significant in favor of treatment by radical mastectomy and irradiation.

Athlete's Foot in Children.—The incidence of athlete's foot in school children was studied by English and Gibson (*Brit. M. J.* 1:1442, 1959). Nearly 4,000 boys and girls aged 11 to 14 and 894 boys aged 7 to 10 were examined clinically and mycologically for dermatophytosis. Of the older boys 40% had lesions of the feet and from 6.6% fungi were isolated. The corresponding figures for the younger boys were 33 and 2.2%, and for the girls 30 and 1.6%. The incidence of dermatophytosis increased gradually to the age of 11 and then fluctuated irregularly. Among the children from whom the organisms were isolated 1.5% were symptomless carriers. No correlation was found between infection rate and personal cleanliness, social class, or the use of school showers. By far the most common infecting fungus was Trichophyton mentagrophytes, which caused 84% of the infections. Trichophyton rubrum was responsible for 7.2% and Epidermophyton floccosum for 4%.

There was a close correlation between infection and proximity of the schools attended by the children to swimming pools. It was concluded that the local swimming pool is an important focus of fungal infection. T. mentagrophytes was, in fact, repeatedly isolated from the floors of these pools. The fungus was found more often in pools used by children with a high incidence of dermatophytosis than in those used by children with a lower incidence. Spread in swimming pools was thought to be by infected fragments of skin pressed on the foot while walking over contaminated floors. Members of the swimming pool staff whose duties entailed their entering the water were also found to be infected. Almost continuous cleaning and sluicing would appear to be the only practical ways of preventing infection from these pools.

Infective Hazards of Water Closets.—Experiments made by Darlow and Bale have shown that flushing a wash-down type of water closet can produce a bacterial aerosol of sufficient magnitude to be an infective hazard (*Lancet* 1:1196, 1959). Any process involving splashing or frothing produces droplets, which remain suspended in the air for a variable period, depending on the mass and evaporation rate of the droplets, and the velocity and direction of local air currents. If the liquid contains solid matter in solution or suspension, an aerosol of droplet nuclei will persist after the evaporation of the rest of the droplet, and may be infective. It is not unreasonable to expect that some fecal pathogens can produce infection by inhalation. Furthermore, excreta may contain causative organisms of diseases that affect systems other than the gastrointestinal tract, such as Mycobacterium tuberculosis, poliovirus, and the Coxsackie and ECHO viruses. The authors demonstrated that the flushing of a water closet generates sizes of particles capable of penetrating to the lower respiratory tract as well as of deposition in the nose, mouth, eyes, and on surfaces touched by the hands.

Experiments were carried out with Serratia marcescens as a test organism for the inoculation of an experimental water closet. A sampling apparatus was mounted at varying levels above it. The maximum number of colonies found on the test plates after flushing was 4,000, representing a mean of 2,000 particles and 19,000 organisms per cubic foot of air. The persistence and wide dissemination suggested that many of the particles were small and tended to remain airborne. It was calculated that about 4,500 particles escaped into the room at each flushing. Aerosol formation was not prevented by the use of the weak disinfectants normally employed in the home.

Family Doctor Center.—On June 1 the Family Doctor Center, at Livingstone House, Edinburgh, was opened. Its object is to provide diagnostic facilities for general practitioners in the area, so that they can deal with some patients whom they would otherwise have to send to the local hospitals for diagnosis and, perhaps, treatment. They will be able to bring any patient to the center whom they would like to investigate more fully than their office hours and facilities would normally permit. The center provides a full range of diagnostic facilities. Its use will be restricted to 40 doctors to avoid overtaxing its resources. This number was selected by ballot from over 100 physicians who applied to use the center. If the center is a success others may be built to increase the facilities of doctors in the National Health Service (NHS). The staff consists of an administrative secretary, stenographer, nurse, laboratory technician, medical social worker, radiographer, part-time radiologist, and part-time medical adviser. The center has fully equipped examination rooms, a clinical laboratory, an x-ray room, and an electrocardiograph.

This center should help to remedy one of the defects in the NHS. Many doctors are frustrated because they cannot get tests done on patients without putting them through the diagnostic routine of the big hospital. Often a physician requires only a simple x-ray or a follow-up blood test on a patient, which he cannot get from the hospital except in an emergency, without a long wait. Confirmation of a general practitioner's diagnosis is often delayed for weeks because the patient is referred to a hospital outpatient service, where diagnostic tests may be done at the rate of one a week.

The new center will give the required diagnostic information within a few hours and will provide facilities for the chronically ill, particularly the patient who is mentally ill, or has a multiplicity of symptoms and visits the doctor frequently. Then the medical social workers will be able to help. It is also hoped that the center will bring family doctors together to discuss their diagnostic problems. It is housed in the premises of the general practice teaching unit of Edinburgh University and should thus provide a link between the medical students and general practitioners there.

Temperature of the Brain During Hypothermia.—The safe duration of circulatory arrest in cardiac surgery under hypothermia is limited by the viability of the central nervous system, particularly the vital centers in the brain, the lower the temperature the longer being the time available. The temperature of the brain at the moment that blood flow to it is stopped is the all-important factor in determining the safe period of circulatory arrest. Hitherto, it has been assumed that the temperature of the brain substance is close to that of the nasopharynx or lower third of the esophagus, but this has never been demonstrated.

Hercus and co-workers (*Brit. M. J.* 1:1435, 1959), using an electric thermometer, took simultaneous temperature readings of the rectum, lower third of the esophagus, nasopharynx, right atrium, and cerebral cortex in sheep. A small drill hole was made in the skull to reach the brain, and the right atrium was reached by passing a cardiac catheter through the jugular vein. The body temperature was lowered to 29 or 30 C by immersion in iced water kept at 1 to 2 C. Over the range 29 to 32 C the temperature recorded in the lower third of the esophagus approximated closely to that of the brain. Rectal and nasopharyngeal temperatures did not show such close agreement, as they reflected changes in blood and brain temperatures sluggishly. Under the condition of the test the rectum required 15 to 20 minutes to reach a stable temperature, whereas the central blood, esophagus, and brain temperature became stabilized in five minutes. The aortic blood temperature was always within 0.2 C of the temperature in the lower esophagus. This close correlation between the temperature in the lower third of the esophagus and the cerebral cortex makes it the logical site from which to record the body temperature during operations under hypothermia.

CORRESPONDENCE

THE HOSPITAL SHIP CONSOLATION

To the Editor:—As one who has spent much time in the Far East teaching and helping set up psychiatric work in China, the Philippines, Indonesia, and Thailand (I am returning to Bangkok in November for another four months of teaching at the medical schools there) and as one who has spent the last 38 years teaching psychiatry at Harvard, New York University, and the University of California, where I have taught many doctors from the Far East, I have been much interested in the announcement of the project to spend $3,500,000 to put the hospital ship Consolation into shape and to send a group of physicians, nurses, and public health workers to the Far East, mainly Indonesia.

I would like to register my own feelings about spending $3,500,000 to send this hospital ship to Indonesia. Just lately I heard that two additional ships may be taken out of mothballs next year and sent to the Far East. It is difficult for me to see what lasting good will be accomplished by a project of this sort, whereas it is obvious that the spending of this amount of money to carry out long-term steady work in these places in the Far East would yield many times the good results of sending a hospital ship. It seems possible to me that sending a ship like this may even have the opposite effect from that desired. It is a sort of spectacular grandstand play showing the great wealth and medical facilities of the United States, but how much good actually will be done in the treatment of sick people and how much can thus be done in the way of medical and nursing education in countries such as Indonesia?

For $3,500,000 one could build an excellent medical school with hospital facilities and staff it with teachers for several years—surely something that would have much more lasting value than the hospital ship. I must confess my feeling that this sort of gesture is something that will give emotional satisfaction to some Americans, including many of those participating in the project, rather than do lasting good in Indonesia.

Probably now it is impossible to reconsider and study whether this same amount of money can be used to better advantage in some other project. I do find it difficult to understand why a scheme of this sort should have been rushed into without getting the opinions of some of the doctors who have training and experience in medical work in the Far East and are most qualified to help evaluate what would be the best way to spend such a large sum of money.

Even if it is too late to stop or change this project, it is not too late to plan for a good evaluation of it and to consider carefully the worth of any continuation of this project or the launching of similar ones. Although it seems to me that it would be difficult to estimate the final results of a project of this sort because the native countries and groups involved will be extremely polite and will not openly express any criticisms which they may have, I do believe it is most important that such an evaluation be attempted and that no further projects be activated without an evaluation and a comparison of the use of a hospital ship with other ways the money might be spent.

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To the Editor:—I am delighted to read of the interest and support which the American Medical Association is giving to the "People to People" program between the United States and other countries, but I cannot refrain from voicing some apprehension with regard to the form which this support is taking. I refer to the use of the hospital ship Consolation as a sort of floating medical center and hospital visiting "Southeast Asia." To outfit and run the ship for one year will require $3,500,000.

This amount of money would go far in equipping a permanent medical school, in underwriting visiting teams going over to stay at the medical schools, and in giving advanced training to potential faculty from the foreign country. While perhaps not as dramatic and spectacular, I believe the latter style of educational program would have more lasting effect and in many ways be more acceptable as well as practical.

Except for the health services of the smaller islands (and these needs are now met by our Navy, the British, and the French, as the responsibility lies), a visit by a hospital ship is hardly the best approach for an educational program. From our experience, short, quick visits from American faculty are of little permanent value. I fear it would be little more than a traveling clinic. It could alleviate many of the immediate and acute illnesses but this is a drop in the bucket compared to the over-all health problem presented by the more populous countries of Southeast Asia. Those problems will best be solved by well-trained native health professionals and by long-term investment in education in medicine and public health. At best, the educational programs under Point IV are too much of an impact phenomenon and do not recognize the need for a slower or sounder approach and maturation.

I believe that the psychological effect of a hospital ship will, on the one hand, tend to separate our visiting group from the host nationals and, on the other, may prove somewhat confining for the morale of the long-term American staff. The matter of language and customs poses many problems in dealing with the sick, whether ambulatory or hospitalized. I am sure it will require much aid from our foreign service personnel. It is conceivable that in some areas it will not be welcome. If I have one suggestion, it is that this well-meaning group consult the China Medical Board or the Rockefeller Foundation before they invest so much money on this type of program.

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FAMILIAL RECURRING POLYSEROSITIS

To the Editor:—The editorial in The Journal, June 6, 1959, page 678, entitled "Is Familial Periodic Disease a Nosological Entity?," calls attention to a remarkable disease largely limited to persons of the Armenian, Syrian, or Jewish ethnic groups. In support of this concept of a "nosological entity" we should like to bring attention to our study of 20 such patients, presented before the annual session of the American College of Physicians, April 21, 1959. We have added to the nomenclature of the disease "familial recurring polyserositis." The nomenclature of the disease has had interesting historical deviations. First called a "paroxysmal syndrome" by Janeway and Mosenthal in 1908, it was termed "benign paroxysmal peritonitis" by Siegal in 1945. Reimann included it in his collection of periodic diseases and added "periodic abdominalgia" or "periodic peritonitis."

French authors have objected to the connotation of "periodic," and Siguier in 1953 called the disease "la maladie dite périodique" (so-called periodic disease). The attacks do not always recur regularly but often recur at grossly irregular intervals from a few days to several months. Mamou coined the term "épanalepsie Méditerranéene," meaning recurring Mediterranean attacks. Bickel in Geneva reverted to the eponym of "la maladie de Siegal-Cattan-Mamou." In 1955 Heller in Israel added "familial Mediterranean fever." He has based his *sine qua non* for diagnosis on the attacks of fever. We have observed patients without fever during episodes of severe pain associated with serositis of the peritoneum, pleura, or synovia; hence we object to the use of a physical sign (fever) as the title of this disease. We also object to the implication of a geographical predilection in the title of this disease. The familial predilection is to certain ethnic groups rather than to any geographical area. In Lebanon the disease is called simply "Armenian disease."

Perhaps, in the future, further knowledge of the pathogenesis of the disease may reveal a biochemical concept such as the possible relationship of etiocholanolone to periodic fever as described by Bondy. Meanwhile, it is suggested that the term "familial recurring polyserositis" avoids the pitfalls of naming the disease for a geographical area, or a physical sign, and avoids the erroneous connotation of regular periodicity. On the basis of present knowledge, polyserositis most accurately characterizes the clinical nature of this disease with findings derived from involvement of multiple serous membranes, e. g., peritoneum, pleura, synovia, or meninges. Interestingly, no patients have been reported from America with the renal involvement so prominent in foreign reports. We believe that "familial recurring polyserositis" is an autonomous clinical entity and deserves to be removed from the group of so-called periodic diseases.

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URINARY INFECTIONS

To the Editor:—The report by Lattimer and co-workers (The Journal, June 20, p. 938) on the serious problem of urinary infections due to resistant strains of Aerobacter aerogenes merits attention. In considering the use of kanamycin as a preferred method of therapy in such infections, one must bear in mind the reports of impaired hearing that have been attributed to kanamycin (Lustberg, A., and Hamburger, M., *J. A. M. A.* 170:806 [June 13] 1959; Naunton, R. F., and Ward, P. H.; *A. M. A. Arch. Otolaryng.* 69:398 [April] 1959; and Damuth, H., personal communication).

It therefore seems appropriate to direct the attention of the readers of The Journal to the study by Hughes and co-workers (*J. Urol.* 80:75 [July] 1958) in which cycloserine appeared to be "of value in the management of chronic urinary tract infection on an outpatient basis, particularly those infections due to A. aerogenes." However, the use of cycloserine, too, is attended with the risk of toxic reactions, a risk which may be minimized with appropriate regulation of dosage.

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MISCELLANY

USE OF HOMOGRAFTS DISPENSED BY CENTRAL ARTERY BANK OF CHICAGO HEART ASSOCIATION

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In August of 1955 the Central Artery Bank of the Chicago Heart Association issued its first lyophilized human vascular segments for transplantation to patients. Under the direction of the cardiovascular surgery committee of the Chicago Heart Association this bank has supplied vascular segments to surgeons throughout the Chicago area for three and one-half years. It is the purpose of this report to review the operations of the Central Artery Bank from Aug. 1, 1955, to Dec. 31, 1958, and to present the results of the use of these grafts in patients.

Three hundred thirty-six homografts have been utilized in patients during this period. All of the vascular segments were obtained at autopsy under carefully controlled conditions. The arteries were sterilized chemically, lyophilized, and stored at room temperature in sealed glass tubes under a vacuum. The methods of obtaining and preparing arterial homografts have been well standardized, and it is not necessary to outline in detail the procedures involved.

With each graft dispensed to a surgeon, a form sheet was attached requesting information regarding the patient, diagnosis, type of operation in which the graft was utilized, and the results of operation. Additional forms were sent to each surgeon at six-month-intervals requesting follow-up information. All expenses of the operation of the Central Artery Bank were borne by the Chicago Heart Association, and the arteries were dispensed without cost to the surgeon, the hospital, or the patient. Special mention is made of the American Red Cross unit in Chicago, which has provided delivery service from the Central Artery Bank to all of the hospitals in which the grafts have been used.

Results in Three Hundred Thirty-six Homografts

The basis of this report is the information obtained from the 38 surgeons in the Chicago area who have used these grafts at operation. The data obtained are presented in categories designated by the type of case in which the graft was used.

Temporary Aortic Cuff.—Fourteen segments of homografts were sutured to aortas to permit inflow from pump-oxygenators and were removed at the end of the procedures, with satisfactory results. None has been used for this purpose since February, 1958, however, and it is likely that the procedure has been discontinued. The principle of using a cuff for access to the aorta may have limited application in certain types of cardiovascular operations.

Roof for Right Ventricle.—One homograft was used for enlarging the right ventricular outflow tract in infundibular stenosis in the period covered by this report. The homograft appears to have certain advantages over the plastic or fabric prostheses for this purpose and will be used in additional similar cases.

Inguinal Hernia Repair.—Two segments of aortic homografts have been used for additional abdominal wall support in two cases of inguinal hernia. The reporting surgeons have indicated that immediate results have been satisfactory and that addition grafts will be used in this manner.

Artery Involved in Tumor.—Three cases of replacement of blood vessels (arteries) involved in tumors have been reported. In two of these cases segments of the abdominal aorta were resected and replaced with homografts. One segment thrombosed one year after operation; the other was reported to be satisfactory at six months, after which the patient was lost to follow-up. In the third case the internal carotid artery was resected and replaced with immediate satisfactory results, but no subsequent reports were received.

Arterial Trauma.—Four cases of resection and replacement with homografts due to trauma to segments of peripheral arteries were reported. Three cases were reported as having satisfactory results with patent grafts up to one year after operation. In the fourth case there was a rupture at the suture line immediately after operation, and the homograft was replaced by a plastic prosthesis.

Superior Vena Cava Obstruction.—Four cases of replacement or bypass of obstructed superior vena cava were reported. In one case of obstruction due to carcinoma, the patient died two weeks after operation. At autopsy the graft was found to be patent and apparently functioning satisfactorily. In each of the remaining three cases bypass of inflammatory strictures of the superior vena cava was carried out. One graft was patent and functioning well one year after operation. One graft remained patent two years, then thrombosed following an accident. The third graft thrombosed three weeks after operation.

Aneurysm of Abdominal Aorta.—Sixty-one cases of resection of aneurysm of abdominal aorta have been reported. In three cases the segments of aorta including the renal arteries were replaced with homografts. These three patients died in the immediate postoperative period of causes unrelated to the grafts.

Seventeen of the patients with aneurysms were operated on as emergencies for acute rupture. Thirteen of the patients died in the immediate postoperative period, three because of disruption of the proximal suture line. It could not be determined whether these three disruptions were associated with defects in the grafts, faulty suturing techniques, or difficulties with the proximal part of the aorta, although the last possibility is perhaps the most likely.

There were 41 resections of aneurysms involving the aorta below the renal arteries; these patients were operated on electively. There were eight deaths unrelated to the grafts, of which seven occurred in the immediate postoperative period and one occurred 12 months after operation. Three deaths were related to the grafts, all occurring in the immediate postoperative period. One of these deaths was due to thrombosis of the graft with extension of the thrombus into the renal arteries. The other two deaths were due to disruption of the proximal suture line.

Of the patients with aneurysms operated on as emergencies, the four surviving patients are well 6 to 16 months after operation. Of the patients operated on electively, 30 are well 6 to 36 months after operation.

Aneurysm of Thoracic Aorta.—Seven cases of resection of aneurysm of the thoracic aorta were reported. Four of these patients died in the immediate postoperative period of causes unrelated to the grafts. Three patients are well more than 24 months after operation.

Aneurysm of Peripheral Arteries.—Nineteen cases of resection of aneurysms of the peripheral arteries were reported.

There was one aneurysm in a vein graft used to replace the femoral artery. This patient is well nine months after replacement with a homograft.

Two aneurysms of the iliac arteries were resected and replaced with homografts. One of these patients died in the operating room of cardiac arrest. The other patient has been well for 18 months since operation. One patient with an aneurysm of the subclavian artery is well 24 months after operation. One patient with an aneurysm of the axillary artery is well six months after operation.

Five aneurysms of the popliteal arteries were resected and replaced with homografts. One graft thrombosed 18 months after operation. One patient died of a myocardial infarction 18 months after operation with the graft functioning well up to that time. Three patients have been well 12 to 18 months since operation.

Ten aneurysms of the femoral arteries were resected and replaced with homografts. Two of the grafts thrombosed, one at one week and one at three months after operation. One graft ruptured at the proximal suture line. There was one wound infection with subsequent rupture at the proximal suture line. Six patients are well six to 24 months after operation with grafts functioning well.

Coarctation of Aorta.—In 22 cases homografts were used in repair of coarctation of the aorta to bridge the resected segments. Two children with preductile coarctations died immediately after operation of causes unrelated to the grafts.

Of 20 cases of postductile coarctations, two patients died in the immediate postoperative period. One patient died of septicemia, with the offending organism being cultured from the graft at autopsy. The second patient died after rupture of the graft at the site of a focus of bacterial endarteritis. The possibility of contamination of these grafts during the processing has been a cause of ever-present concern. However, cultures are taken routinely and since the bank has been in operation not a single positive culture has been returned. The remaining 18 patients are well 6 to 36 months since operation. This group of patients should be especially valuable for long-term follow-up, since all of the patients are children or young adults in good health.

Transposition of Great Vessels.—Partial correction of transposition of the great vessels with grafts from the inferior vena cava to the left atrium was reported in 71 cases. There were 29 deaths in this group, none of which was related to the grafts. The remaining 42 patients are well from a few weeks to 24 months after operation, with the grafts apparently functioning well in all the patients.

Aortic Bypass, Occlusive Disease.—Forty-one cases of aortic bypass for arteriosclerotic occlusive disease were reported. There were five deaths in this group which were unrelated to the grafts. Thrombosis of one or both limbs of bifurcation grafts occurred in 11 cases, from one week to one year after operation. In 25 cases the grafts have been functioning well from 6 to 36 months after operation.

Aortic Resection, Occlusive Disease.—Fifty-five cases of resection of the abdominal aorta for arteriosclerotic occlusive disease have been reported. There were nine deaths in this group, of which five were not related to the graft. The other four deaths were due to thrombosis of the grafts with extension of the thrombi into the renal arteries. Thrombosis of one or both limbs of bifurcation grafts occurred in five cases, four days to 18 months after operation. Forty-one patients in the group are well with functioning grafts 6 to 36 months after operation.

Resection or Bypass, Occlusive Disease of Peripheral Arteries.—Twenty-seven cases of bypass or resection of peripheral arteries for arteriosclerotic occlusive disease were reported.

There were 10 cases of iliofemoral bypass. In six of these cases the grafts thrombosed from one day to one year after operation. One patient was discharged 10 days after operation with the graft functioning well, but was lost to follow-up thereafter. In three patients grafts are functioning well 15 to 36 months after operation.

There were five cases of iliopopliteal or femoropopliteal bypass. In these five patients the grafts thrombosed, 3 to 12 months after operation.

In three patients segments of the femoral artery were replaced with homografts. Two of the grafts thrombosed, 6 and 15 months after operation. In the remaining patient the graft has functioned well 12 months after operation.

Femorofemoral artery bypass was carried out in nine patients. In seven of these patients the grafts thrombosed immediately or up to five months after operation. In the remaining two patients the grafts have been functioning well 6 and 24 months after operation.

The number of arterial homografts used at operation during the individual years is of some interest. In 1955, 23 homografts were implanted into patients; in 1956, 105 homografts; in 1957, 124 homografts; in 1958, 84 homografts. During the last six months of 1958 only 27 homografts were used. This decrease in demand for the homografts, of course, reflects the increasing preference of many of the surgeons for the synthetic grafts. At present, the greatest demand for homografts from the Central Artery Bank is in the partial correction of transposition of the great vessels. For this procedure the synthetics have not proved to be as satisfactory as the homografts.

It is our opinion that the data presented here indicate that the Central Artery Bank of the Chicago Heart Association has fulfilled the purpose for which it was organized in 1955. Special demands for the homografts continue, and as long as a reasonable number of the grafts are utilized the operations of the bank will be continued. Long-range studies on homografts and on the synthetic fabrics are as yet inadequate, and the final dispositions of both types of grafts are not yet determined.

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STATEMENT OF PRINCIPLES OF ETHICAL DRUG PROMOTION

The Pharmaceutical Manufacturers Association, which was formed in 1958 by the merger of the American Drug Manufacturers Association and the American Pharmaceutical Manufacturers Association, now represents some 140 manufacturers of pharmaceutical products. The board of directors of the Pharmaceutical Manufacturers Association recently adopted the following statement of principles of ethical drug promotion:

We, members of the Pharmaceutical Manufacturers Association, recognizing our responsibilities and obligations to promote the public welfare and to maintain honorable, fair, and friendly relations with the medical profession, with associated sciences, and with the public, do pledge ourselves to the following statement of principles:

1—Prompt, complete, conservative and accurate information concerning therapeutic agents shall be made available to the medical profession.

2—Any statement involved in product promotional communications must be supported by adequate and acceptable scientific evidence. Claims must not be stronger than such evidence warrants. Every effort must be made to avoid ambiguity and implied endorsements. Whenever market, statistical or background information or references to unpublished literature or observations are used in promotional literature, the source must be available to the physician upon request.

3—Quotations from the medical literature or from the personal communications of clinical investigators in promotional communications must not change or distort the true meaning of the author.

4—If it is necessary to include comparisons of drugs in promotional communications, such comparisons must be used only when they are constructive to the physician and made on a sound professional and factual basis. Trademarks are private property that can be used legally only by or with the consent of owners of trademarks.

5—The release to the lay public of information on the clinical use of a new drug or to a new use of an established drug prior to adequate clinical acceptance and presentation to the medical profession is not in the best interests of the medical profession or the layman.

6—All medical claims and assertions contained in promotional communications should have medical preview prior to their release.

7—Any violation of these principles brought to the attention of the President of the Pharmaceutical Manufacturers Association shall be referred by him to the Board of Directors.

These principles were brought to the attention of the Board of Trustees of the American Medical Association at its meeting in Atlantic City. The Board commended the P. M. A. for adopting these principles for ethical drug promotion.

MEDICAL LITERATURE ABSTRACTS

SURGERY

Microscopic Phaeochromocytoma of the Adrenal. P. B. Desai. Indian J. Surg. 21:1-7 (Feb.) 1959 [Madras, India].

The author reports on a 59-year-old man with a microscopic pheochromocytoma in a normal adrenal. The patient was admitted to Tata Memorial Hospital in Bombay, India, because of paroxysmal attacks of headache for one year, unstable blood pressure, pigmentation of the face, and intermittent attacks of vomiting. The blood pressure used to range from 225/135 mm. Hg to 180/100 mm. Hg during the attacks. The basal blood pressure was about 140/80 mm. Hg. An ill-defined round opacity above the left kidney shadow was revealed by a plain roentgenogram of the abdomen. Retroperitoneal pneumography showed a well-rounded shadow, presumably the suspected pheochromocytoma, above the left kidney. The patient was explored by a left-sided thoracoabdominal approach along the 11th rib. Immediate elevation in the blood pressure was observed whenever the left suprarenal area was palpated. A similar manipulation of the right adrenal did not produce any change in the blood pressure. This significant observation led to the decision to remove the left adrenal, although it appeared normal. It was only accidentally discovered that the shadow in the roentgenogram above the kidney region was caused by a cartilaginous patch of thickening on the pleural surface of the diaphragm. The postoperative recovery of the patient was uneventful. The blood pressure showed a sustained drop.

Microscopic examination of the operative specimen showed the distinct contrast between the normal and the tumor tissue of the adrenal. The tumor cells were large with clear cytoplasm, multinucleated, and arranged in cords and sheets, typical of pheochromocytoma. The patient has been followed up for 6 months postoperatively, and he has not had a single attack of headache and rise of blood pressure. His blood pressure now varies from 140 to 160 mm. Hg systolic and from 80 to 90 mm. Hg diastolic. He can, with sufficient reason, be called cured. The significance of sudden elevations of blood pressure, during manipulation of the adrenal gland concerned, in betraying an invisible pheochromocytoma within a seemingly normal and innocuous adrenal, is emphasized. This is a definite indication for removal of that adrenal.

The Treatment of Parosteal Osteoma of Bone. M. M. Copeland and C. F. Geschickter. Surg. Gynec. & Obst. 108:537-548 (May) 1959 [Chicago].

The authors report observations on 22 patients with what they designate as parosteal osteoma, a newly recognized bone tumor which has been designated by others as parosteal osteogenic sarcoma. The new entity occurs in both benign and malignant forms and is seen most frequently in the first 4 decades of life. In 10 of the 22 patients the lesions were found on the posterior surface of the lower femur, bulging into the region of the popliteal space. Similar growths were observed about the upper femur, upper and lower portions of the humerus, upper ulna and radius, upper fibula, and lower tibial regions. The group of patients included 12 females and 10 males. A swelling or mass and local pain or tenderness were the outstanding clinical features. Ten of the patients had noticed a mass for one year or more. One patient had noticed an increasing enlargement of her lower thigh for 7 years. In one patient, irradiation for skin disease preceded the bone lesion by 32 years.

On examination, a mass of bony hardness is felt, which is firmly attached to the adjacent bone. The periphery of the bony mass is usually smooth in contour. On roentgenologic examination, a mass, densely ossified, circumscribed, frequently sharply outlined, and occurring outside the bone but contiguous with it, is usually visible. At operation, the mass is found fused with the periosteum, with pseudoencapsulation often seen at its outer margins. Grossly, on section, the tumor has a firm, dry, striated surface much like fibrosed cancellous bone. Microscopically, although adult bone and fibrous tissue predominate, foci of cartilage cells may be seen. At the periphery the growths are more apt to show increased cellularity and, in a number of cases, have shown features of fibrospindle-cell sarcoma.

Of the 22 cases reviewed, 16 had been previously described by the authors. Observations on these and on 6 new cases emphasize the fact that paros-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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teal osteomas are potentially malignant lesions. The original lesion appeared to be benign in 14 of the 22 patients. Subsequent surgery, necessary for recrudescence, revealed the tumor as benign in only 2 cases at the second operation. The tissue removed in the only or final operation was considered malignant in 15 instances, benign but cellular in 3, and typically benign in 4. Of 18 patients with determinate reports, 11 are living and well 5 or more years after resection (excision) or amputation. Eight of these patients are living and well for from 7 to 25 years after treatment, while 3 lived 5 or more years and then died of metastases. In 8 of 13 patients the disease recurred after local excision or resection, and amputation was necessary. Five of the 8 patients died of their disease, while 3 are living and well after 5 years or more. Three primary amputees are 5-year survivals, without disease.

Ablative surgery by resection or amputation is necessary to cure parosteal osteoma, in the majority of cases. If complete resection in a relatively inactive lesion can be accomplished, cure should result. There is no place for temporizing surgical excisions. If there is any question about adequate en bloc resection, then amputation is indicated. When pathological changes show frank sarcoma, amputation is indicated at once. Recurrent cases, with or without malignant manifestations, are best treated by amputation. Parosteal osteoma must be differentiated from (1) localized myositis ossificans, (2) intraligamentous osteoma or osteoma of the tendon sheath, (3) sclerosing osteogenic sarcoma, and (4) osteochondroma and exostosis. The differentiating features are discussed.

Observations on Hepatitis Associated with Biliary Lithiasis: Histopathological and Clinical Studies on 90 Cases. B. Kourias and N. Papacharalampous. Lyon chir. 55:179-190 (March) 1959 (In French) [Paris].

The authors carried out histopathological studies on liver specimens obtained from 90 patients who had undergone surgery (87 for cholecystitis, with or without lithiasis, and 3 for duodenal ulcer); the object was to find out whether alterations had taken place as a result of the primary disease. The histological examinations were made on both superficial and deep liver specimens obtained by aspiration biopsy. The findings of these examinations showed that there were neither superficial nor deep lesions in 6.9% of the patients, but both superficial and deep lesions were found in 48.8% of the patients. The lesions were severe in 22.7%, moderate in 54.5%, and mild in 22.7%. The deep lesions were much less severe than the superficial ones in 26.6%. The lesions were localized exclusively in the superficial region in 18.6%. Thus, lesions have been found either in the hepatic cells or in the interstitial tissue, or in both, in 93.1% of the patients. The deep lesions should be considered more important than the frequently occurring lesions of the liver cortex. The most serious lesions were noted in patients with jaundice, but no correlation could be established between the duration of the disease and the seriousness of the lesion. A marked inconsistency was observed between the liver function tests in these patients and the extent of the hepatic lesions.

There were 2 deaths. The rest of the patients were followed up for from 1 to 3 years; the results were generally satisfactory even in those who had had severe hepatic disease. This study warrants the conclusion that cholecystectomy or concurrent drainage of the common bile duct will lead to regression of the hepatic lesions in most patients.

Acute Arterial Occlusion of Extremities: Study of 20 Cases. H. M. Coelho, J. Fernandes Oliveira and P. M. Garcia. Rev. paulista med. 54:167-176 (March) 1959 (In Portuguese) [São Paulo, Brazil].

Twenty patients with acute peripheral arterial occlusion were observed during 1957 at the Faculty of Medicine of the University of São Paulo. Observations were made either until death or for more than a year after discharge from the hospital. The period of time which elapsed between the appearance of occlusive symptoms and hospitalization varied between 2 hours and 7 days in 19 patients; in one patient, however, it was 5 months. The occlusion was caused by an embolus in 18 patients, by repeated arterial trauma during intra-arterial blood transfusion in one, and by a dissecting aneurysm of the aorta and right iliac artery in one. Most of the patients who had had rheumatic fever developed embolism between the ages of 40 and 50 years, whereas those with hypertension, arteriosclerosis, and myocardial sclerosis developed it between 55 and 82. The occluded arteries were the axillary in 4 cases, brachial in 3, iliac in 4, femoral in 5, and popliteal in 2, as well as the bifurcation of the aorta in 5. The total number of involved limbs was 28, because of the presence of bilateral or multiple emboli in some cases. Most of the patients were hospitalized in grave condition. Two entered in coma, with severe cardiac disease, multiple embolism, and the legs in cadaveric rigidity; they died of cerebral embolism 5 and 24 hours, respectively, after hospitalization. In the remaining 18 patients there was acute or moderate ischemia in 11 limbs, muscular induration in 5, necrosis in 1, and gangrene in 4. Preoperative treatment consisted of drugs to correct heart decompensation, shock, anemia, dehydration, and decompensated diabetes.

Seven patients had an embolectomy, and arterial circulation was reestablished in the limbs of 5, since the operation was performed within 8 hours after the appearance of occlusive symptoms. An amputation was performed in the case of 3 patients with gangrene; 2 of these patients died. Conservative treatment, consisting of sympathetic blockage and intravenous injections of heparin in doses of 75 or 100 mg. at intervals of 4 hours, was given to 8 patients, with good or fair results in 6; in the remaining 2 patients the treatment was followed by the appearance of gangrene, which called for amputation. Of the 20 patients in this series, there was an operative mortality from embolectomy or amputation in 4 patients, and death occurred as a result of embolism or gangrene in 7. Nine patients are surviving in a satisfactory or fair condition one year after discontinuation of the treatment. The best results were obtained in those who were treated not later than 8 hours after the appearance of occlusive symptoms.

Needle Biopsy of the Liver During Abdominal Surgery. R. B. Terry. Am. J. Digest. Dis. 4:378-388 (May) 1959 [New York].

The author describes an instrument which has been found suitable for needle biopsy of the liver during abdominal surgery. In patients with abdominal carcinoma in whom hepatic nodules are found, liver biopsy becomes imperative. Such hepatic nodules are often difficult to assess by inspection and palpation. In a proportion of cases unnecessarily palliative surgery may be performed, and gross errors in prognosis made, if hepatic nodules are not examined histologically. Biopsy of the liver by wedge resection during abdominal surgery is occasionally attended with difficulty and may fail to obtain satisfactory tissue because of the atypical nature of the free margin of the liver; for these and other reasons, it is frequently not performed when indicated. Needle biopsy of the liver during abdominal surgery is simple and rapid; any bleeding is easily controlled, and the specimen obtained is not only adequate in size but contains fewer artefacts than that obtained by wedge resection. The author performed 35 biopsies with the biopsy instrument during abdominal surgery. The material proved to be adequate for diagnosis. There was no difficulty in controlling bleeding, which in many instances was remarkably slight, and no complications were encountered in the series. The mortality rate for "medical" or percutaneous biopsies of the liver has been 0.12% among 10,600 biopsies reported in the literature, while the incidence of significant complications has been 0.38%. There would presumably be far less trouble with needle biopsy of the liver performed during abdominal surgery.

GYNECOLOGY & OBSTETRICS

Endometriosis Involving the Pleura. C. B. Ripstein, M. Rohman and J. B. Wallach. J. Thoracic Surg. 37:461-471 (April) 1959 [St. Louis].

The authors report on a 24-year-old woman with endometriosis involving the pleura. The patient had recurrent hemorrhagic effusion, increased menses associated with moderate abdominal pain, and inability to conceive. The diagnosis was considered clinically and was confirmed by histological examination of tissue from the pleural and peritoneal cavities. Diagnostic pneumoperitoneum was followed promptly by pneumothorax, indicating the presence of a communication between the pleural and peritoneal spaces on the right and permitting the application of the implantation theory in explanation of this unusual site of endometriosis. The cases of only 2 patients with pleural endometriosis and 1 with endometriosis of the lung have so far been reported in the literature. This pathological process should be considered in a young woman with recurrent hemorrhagic pleural effusion of obscure etiology. Early treatment directed at suppression of ovarian function will provide relief of the debilitating symptoms secondary to the continuing accumulation of the irritating bloody fluid in the pleural space.

Combined Radiologic-Surgical Treatment of Carcinoma of the Cervix. T. Dahle. Surg. Gynec. & Obst. 108:600-604 (May) 1959 [Chicago].

The author believes that both irradiation and surgical treatment have a place in the therapy of carcinoma of the uterine cervix. This study was undertaken to investigate the anatomic spread of cancer of the uterine cervix in patients with stage 1 lesions, and to analyze the dangers to the ureters in combined radiologic and surgical treatment. Two hundred sixty-six patients with stage I cervical cancer were admitted to the Norwegian Radium Hospital in Oslo in 1954, 1955, and 1956. For various reasons it was not possible to perform radical surgery on all these stage 1 patients and only 96 of them underwent radical surgery and preoperative radium treatment. The material was a selected one, the patients being young and in relatively good condition. The clinical staging was always made under Nembutal anesthesia and the examination of the renal tract always included urinalysis, determination of the blood urea, cystoscopy, and urography. There were 88 cases of squamous- carcinoma and 1 of adenocarcinoma; in 7 cas diagnosis was undifferentiated carcinoma.

All the patients first received radium equivalent to from 6,000 to 7,200 mg.-hr fractions (30 mg. of radium in the va to 30 mg. in the uterus for 5 days selected for combined therapy were teal osteomas are potentially malignant lesions. The original lesion appeared to be benign in 14 of the 22 patients. Subsequent surgery, necessary for recrudescence, revealed the tumor as benign in only 2 cases at the second operation. The tissue removed in the only or final operation was considered malignant in 15 instances, benign but cellular in 3, and typically benign in 4. Of 18 patients with determinate reports, 11 are living and well 5 or more years after resection (excision) or amputation. Eight of these patients are living and well for from 7 to 25 years after treatment, while 3 lived 5 or more years and then died of metastases. In 8 of 13 patients the disease recurred after local excision or resection, and amputation was necessary. Five of the 8 patients died of their disease, while 3 are living and well after 5 years or more. Three primary amputees are 5-year survivals, without disease.

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GYNECOLOGY & OBSTETRICS

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All the patients first received radium treatment equivalent to from 6,000 to 7,200 mg.-hr. in 1 or 2 fractions (30 mg. of radium in the vagina and 20 to 30 mg. in the uterus for 5 days). The patients selected for combined therapy were discharged 1

6 to 8 weeks and then readmitted for radical hysterectomy and pelvic lymphadenectomy. The patients not selected for the combined treatment, immediately after the radium treatment, underwent a complete course of x-ray therapy, including a 3,000-r skin dose to each of 2 anterior and 2 posterior pelvic ports. It is known that the clinical staging of patients with carcinoma of the cervix is often unreliable, and such was the case in this material. In 18 of the 96 supposedly stage 1 patients, metastases were found in the lymph nodes. Since Meigs found lymph node invasion in 17.5% of stage 1 patients treated only surgically, it appeared that radium therapy had no influence on the lymph node metastases. In 16 of the 96 patients, residual carcinoma was found in the cervix, but in 12 of the 18 patients with lymph node metastases, no residual carcinoma was found in the cervix.

No rectovaginal or vesicovaginal fistula resulted, but, when possible, damage to the ureters was examined by means of urography; 69 patients showed no abnormality from 6 months to 1 year after treatment, but 22 did show damage. Four patients are now dead, 3 having died of carcinoma and 1 of bilateral pyonephrosis. It is believed that most of the changes in the urinary tract were caused by the treatment, but in 11 of the patients the hydroureter or hydronephrosis was slight. The possibility of damage to the urinary tract must be borne in mind when reflecting on the value of the combined radiologic and surgical treatment.

Association of Cervical Cancer with Circumcision of Sexual Partner. J. E. Dunn Jr. and P. Buell. J. Nat. Cancer Inst. 22:749-764 (April) 1959 [Washington, D. C.]

There have been reports to the effect that cervical cancer is only one-fifth or less as frequent in Jewish women as in non-Jewish women. Wynder and associates in 1954 reported on data from 2 sources in support of the hypothesis that circumcision of the male is a protective factor. The present authors suggest that other factors might be involved. They present data from a study not designed solely to test the question of circumcision but to study other variables possibly associated with cervical cancer. During the years 1951-1955, 429 patients with cervical cancer were interviewed. The same number of controls were selected by matching on age (within 5 years), race, ever married, and ever parous. A further restriction was made by selecting the patient-control pair from the same hospital (Los Angeles County Hospital) or the same private or group practice. Attention is called to differences in the collection of controls by Wynder. The present authors in their interviews were unable to find an association between having cervical cancer and reporting an uncircumcised husband. Wynder had previously reported an association in a study that also used data on circumcision history obtained from interviews with women patients. There may have been differences in asking the questions about circumcision, but, if so, it is not clear how the data were affected.

An additional independent investigation of circumcision as an anatomic fact revealed that Jewish men probably have a maximum degree of anatomically complete circumcision, which occurs in less than half of non-Jewish men who consider themselves circumcised. The circumcision study also revealed that one-fourth to one-third of men naturally may have a partially shortened foreskin, which is similar to that of some men who have been circumcised, but, in an interview study, many of them will be counted as uncircumcised. Consequently an interview study of non-Jewish subjects may fail to identify the fully circumcised and further dilute the results with many "partially circumcised" classified as uncircumcised. Possibly the problem can be settled only in a study which makes direct examinations of sexual partners to distinguish full and partial circumcision.

The Occurrence of Episodes of Immunization in Pregnancy Associated with Rh Haemolytic Disease of the New-Born. G. A. Kelsall, G. H. Vos and R. L. Kirk. M. J. Australia 1:488-493 (April 11) 1959 [Sydney].

The authors carried out antenatal titrations of antibodies found in pregnant mothers, serums at the King Edward Memorial Hospital for Women in Subiaco, Western Australia, at every available opportunity during the last 7 years. Frequent titrations in the course of pregnancy showed that immunization of the mother occurs as one or more episodes during the pregnancy, and that the resulting antibody titers may be of minor or major magnitude. The prognosis for the fetus depends largely on the Rh-antibody titer. The patterns of antibody behavior were numerous and varied. The findings seem to justify the following conclusions concerning the prognosis for a particular pregnancy and the outlook for later pregnancies. 1. A previously immunized woman may undergo a further incompatible pregnancy without any episode of immunization occurring in the later pregnancy. If the initial titer in such a pregnancy is low, the infant will be mildly affected; if the initial titer is high, the infant may be severely affected. 2. A previously immunized woman may have one or more episodes of immunization in a subsequent incompatible pregnancy. The outcome for the fetus will depend on the number of episodes, the rise of titer, and the duration of a high titer of antibodies. 3. Antibody titers may fall between pregnancies, and sufficient time must be allowed for this to happen. A sensitized woman mated to a homozygous man has a much better chance of having a surviving infant if her titer is low at the beginning of pregnancy.

Antibodies frequently appear for the first time in the last 4 weeks of pregnancy, and they may rise precipitiously to lethal levels in the few remaining weeks of pregnancy. Of 409 immunized mothers, 75 (18%) were free of antibodies when first examined by the authors; antibodies developed in 33 (8%) before 34 weeks of gestation had been completed, and in 42 (10%) antibodies developed after this time. Of the 334 (72%) who already had antibodies when first examined, 113 (25%) had an episode of immunization before 34 weeks, and 196 (45%) had one after 34 weeks' gestation. The premature induction of labor at 36 weeks probably obviated the occurrence of many more dangerous episodes in the last 4 weeks of pregnancy. Induction of labor is not only of value in that particular pregnancy, but must have some bearing on the success of future pregnancies, in that it would tend to keep the mother's titer at a lower postconfinement level and provide a lower antibody "take off" when the next pregnancy begins.

Wertheim Hysterectomy in the Treatment of Endometrial Carcinoma. L. Parsons and F. Cesare. Surg. Gynec. & Obst. 108:582-590 (May) 1959 [Chicago].

In view of the renewed interest in radical dissection of the pelvic lymphatics for cervical cancer, the authors elected to employ the Wertheim type of hysterectomy and pelvic node dissection in the treatment of endometrial carcinoma. This report, based on 62 cases in which treatment consisted of the Wertheim hysterectomy, is presented as a critical study of the many factors underlying the management of endometrial carcinoma by a radical surgical approach. The patients were observed at several hospitals in the area of Boston between 1946 and 1956. There were 52 adenocarcinomas, 9 adenoacanthomas, and 1 carcinosarcoma. Fifty-two were primary cases, while in 10 previous irradiation had been received. Myometrial invasion was present in 37 cases, or 60% of the group. Bilateral pelvic lymph node dissection was carried out in 50 of the 62 patients, while in the remaining 12 no pelvic lymph node dissection was done. Lymph node involvement was observed in 4 of the 50 patients in whom the nodes were dissected, and these 4 belonged to the group of 37 who had myometrial invasion. One of the 4 women died in the hospital, 1 lived 3 years, and 2 are alive and well at 2 years. Complications occurred in 27% of the patients, urinary tract disturbances accounting for 12% of these. Urinary fistulas developed in 5 patients, an incidence of 8%. Etiological factors as well as practical preventive measures are discussed. There was one surgical death (1.6%).

The technique of the Wertheim hysterectomy is briefly described. Of 3 pelvic recurrences, 2 appeared within the first year, but the third not until 3 years after the operation. This latter case is of special interest, having shown both myometrial and lymph node involvement. Two of these patients ultimately died of their disease, while the third is still living and well 6 years after vaginectomy. The 5-year survival can be evaluated in 33 of the 62 patients. Twenty-six of the 33 patients survived 5 years or more without recurrence, an absolute 5-year cure rate of 78%. Two patients are now alive and well 10 years after surgery. The 5-year survival of the primary treatment group was 81% (22 of 27 patients). In the patients with myometrial invasion the 5-year salvage rate was 71%.

The authors feel that the results obtained compare favorably with those reported in the current literature and justify further evaluation of the radical surgical approach for the treatment of endometrial cancer. The high incidence of postoperative complications, however, imposes heavy obligations on those who treat and care for these patients. It is hoped that future experience and observations will add to the knowledge of the metastatic spread of endometrial cancer, improve selection of patients, and reduce morbidity, at which time the Wertheim hysterectomy with pelvic lymph node dissection may prove worthy of more routine use.

Early Cancer Detection: Prediction of Preclinical and Preinvasive Stages by Cytology. J. E. Ayre. Acta Unio internat. contra cancrum 15:289-295 (no. 2) 1959 (In English) [Louvain, Belgium].

In the diagnosis of early preclinical cancer, cell scraping is the method of choice for the collection of material. In examinations on 111,963 patients, 1,874 gynecologic cancers (20.3%), were found by cytology, and 59 were missed, including 22 cervical cancers. Absence of clinical symptoms is inadequate in discarding cancer diagnosis. Comparisons of clinical appearance and cytological findings are presented for preinvasive, early invasive, and infiltrating cancers. Among 347 histologically confirmed cancers, 70 were "cytologically early"; cytological diagnosis of preinvasive nature was confirmed in 70% of the cases. Cell-population studies allowing this diagnosis are discussed.

PEDIATRICS

Sequestration of the Lung. M. C. Buchanan. Arch. Dis. Childhood 34:137-139 (April) 1959 [London].

The author reports on a girl with an abnormal pulmonary artery supplying a sequestrated segment of the lung, who at the age of 8 years was admitted for the first time to the Queen Elizabeth Hospital for Children in Londan for vague symptoms of ill health, such as tiredness, occasional headaches, pain in the limbs, and cough. A chest roentgenogram did not show any evidence of a pulmonary lesion except basal emphysema on both sides. At the age of 11 years the patient was again admitted to the hospital for similar symptoms. In addition, her temperature was 103 F (39.4 C). A chest roentgenogram showed a partial collapse of the right middle lobe and the anterior segment of the lower lobe. Sulfonamide and penicillin therapy was ineffective in controlling the symptoms and the pyrexia. Improvement resulted from treatment with chlortetracycline (Aureomycin), and serial chest roentgenograms showed some resolution of the lesion at the right base, but a tomogram showed cyst-like cavitation in the periphery of the right lower lobe, irregular consolidation, and thickening of the bronchial wall.

After 13 weeks in the hospital, the patient was discharged, only to be readmitted 3 weeks later with anorexia, recurrence of cough, and a temperature of 100 F (37.8 C). A bronchogram was obtained, revealing a lesion whose behavior, site, and appearance suggested a sequestrated lung segment. Excision of the right lower lobe was performed. There was a small mass in the posterior basal segments. Entering this mass from the region of the diaphragm was a vessel about 3 mm. in diameter. Microscopic examination of the operative specimen revealed a small abscess cavity in the posterior subapical area. In the posterior basal region there was an area of lipid pneumonitis containing a number of small abscesses. In the anteromedial portion of the lobe there was a tube-like structure which extended laterally and divided into a number of branches; this was thought to be an ectopic bronchus. Moreover, there was emphysema of the basal segments. After the operation the patient made a complete recovery.

The syndrome of sequestrated lung segment is probably not as rare as is generally believed. The condition is disabling, but it is cured by surgery. There are few symptoms referable to the lungs, minimal physical signs, but gross roentgenologic changes. The condition, once suspected, can be diagnosed before operation. The most likely explanation of its causation in the patient reported is that there was a small communication between the air contained in the surrounding normal lung and the air spaces in the ectopic tissue; this was sufficient to aerate the latter, but it was insufficient to drain the products of infection once the condition had occurred.

Treatment of Diphtheria with Terramycin. H. W. A. Voorhoeve. Maandschr. kindergeneesk. 27:119-132 (April) 1959 (In Dutch) [Leiden, Netherlands].

The incidence of diphtheria has decreased in the Netherlands in recent years, and this has been ascribed to the fact that more children are being vaccinated against it. The mortality of diphtheria, however, has remained about the same, namely, 6%. This persisting high mortality induced the author to evaluate the treatment of diphtheria. He compared 2 groups of 55 patients each, one being treated before 1953 and the other after 1953. The diagnosis was bacteriologically verified in both groups of patients. All were treated with the same type of antidiphtheria serum, which was administered by intramuscular injection in doses of from 20,000 to 40,000 units.

On the basis of a 1953 report by Lall and Karelitz, of New York, on the use of Terramycin in diphtheria (abstracted, J. A. M. A. 153:592 [Oct. 10] 1953), the administration of Terramycin, in addition to antidiphtheria serum, was begun at the Juliana Kinderziekenhuis (Den Haag) in October, 1953. Terramycin was given in daily doses of 50 mg. per kilogram of body weight, divided into 3 or 4 doses, usually by mouth. While the addition of Terramycin to the treatment produced no noticeable change in the mortality from diphtheria, throat cultures became more rapidly negative, so that the children did not have to remain isolated for such a long period and hospitalization could be shortened. On the other hand, it seems probable that with Terramycin therapy the immunizatory effect of the diphtheria is lessened, and so the author feels that patients who have received Terramycin for diphtheria should still be immunized against the disease.

The Antibiotic Management of Staphylococcal Disease in Infants and Children. M. D. Yow, M. M. Desmond and L. N. Nickey. South. M. J. 52:392-400 (April) 1959 [Birmingham, Ala.].

The authors report on 155 infants, aged less than 2 months, 32 babies, between the ages of 2 months and 2 years, and 17 older children, all with staphylococcic infections who were treated with antibiotics at Jefferson Davis Hospital in Houston, Texas, between 1956 and 1958. Eighty per cent of the staphylococcic infections were classified as hospital-acquired, and 20% were considered to be of extra-hospital origin. Sixty-six of the 204 patients had mild disease, and 138 had moderately severe or severe involvement. The antibiotic agents employed were selected on the basis of probability of response until the results of in vitro testing were available. During the first year of this study most of the patients with hospital-acquired infections were treated with a combination of erythromycin and streptomycin, erythromycin and chloramphenicol or chloramphenicol or novobiocin alone (bacteriostatic antibiotics). Disappointing results with these commonly used antibiotics and increasing awareness that a large proportion of these infections were due to the virulent Staphylococcus organisms phage-type 81, led to a trial of bacitracin and kanamycin (bactericidal agents). Both these drugs seemed especially suitable for use in infants and children because of their bactericidal activity and because they could be administered by the intramuscular route. In seriously ill patients all antibiotics were given initially by the parenteral route for a minimal period of 48 hours. Oral therapy was used when the patient began to improve and where it was practical. Local administration of antibiotics was used in localized infections, such as empyema, purulent pericarditis, meningitis, and septic arthritis.

The age of the patients influenced morbidity and mortality. Among the 138 patients with serious staphylococcic disease, the mortality rate was 43% in the premature infants, 26% in the full-term newborn infants, 21% in children from 2 months to 2 years of age, and 12% in older children. The degree of dissemination was related to the age of the patient, demonstrating inadequacy of host defenses in the young infant. The selection of the specific antibiotic agent for the treatment of staphylococcic disease, including impetigo, conjunctivitis, subcutaneous abscess, septicemia, pneumonia, gastroenteritis, meningitis, and miscellaneous conditions, depends on the age and condition of the host. In older children or patients with normal defense mechanisms, mild and moderately severe staphylococcic infections can be expected to respond to treatment with bacteriostatic antistaphylococcic drugs. Controlled studies are needed to establish the best method of management of mild superficial infections in the newborn infant. Even moderately severe infections in the young infant must be considered potentially dangerous because of the infant's inability to localize infection, and this patient should be treated with a bactericidal antistaphylococcic drug. The prognosis of severe staphylococcic disease in all age groups is so grave that intensive therapy with a bactericidal antibiotic or a combination of a bactericidal drug and a bacteriostatic drug is indicated.

Nephrocalcinosis Infantum. R. A. Shanks and A. M. MacDonald. Arch. Dis. Childhood 34:115-119 (April) 1959 [London].

The authors report on 84 cases of nephrocalcinosis observed in children who died at the Royal Hospital for Sick Children in Glasgow and on whom autopsies were performed between 1928 and 1957. Nine cases were observed between 1928 and 1937, 15 between 1938 and 1947, and 60 between 1948 and 1957; these data suggest a true increase in the incidence of this condition. Of the 9 cases, 3 occurred in infants aged less than 1 year, 1 in an infant between 1 and 2 years, and 5 in children over 3 years of age. Of the 15 cases, 9 occurred in infants aged less than 1 year, 3 in children between 1 and 3 years, and 3 in children over 3 years of age. Of the 60 cases, 47 occurred in infants aged less than 1 year, 10 in infants between the ages of 1 and 2 years, and 3 in children over 3 years of age. Thus, 70% of the cases were observed in infants in the course of the first year of life.

A wide variety of pathological conditions, in themselves sufficient to cause death, was found in association with the lesions of nephrocalcinosis in this series of patients. The first and most obvious explanation for these findings is that nephrocalcinosis is a casual autopsy finding seldom related to the cause of death. The virtual absence of the condition in children between 2 and 3 years of age likewise suggests that not only is it usually not fatal but it normally proceeds to complete resolution. The implications, therefore, are that most of the lesions of nephrocalcinosis belong to a benign disorder of infancy without severe symptoms and with an excellent prognosis. The condition is probably related to idiopathic hypercalcemia of infancy.

OPHTHALMOLOGY

The Treatment of Iris Melanoma. A. B. Reese and G. W. Cleasby. Am. J. Ophth. 47:118-125 (May) 1959 [Chicago].

This report is based on 157 cases of melanoma of the iris. They include (1) patients seen and treated at the institute of ophthalmology, Columbia-Presbyterian Medical Center, New York, and Stanford University Hospital, San Francisco; (2) patients seen in consultation by members of the staff of the institute of ophthalmology but treated elsewhere; and (3) patients operated on elsewhere, whose tumor specimens or sections were sent to the pathology department of the institute of ophthalmology for opinion. From the standpoint of treatment the 157 patients fall into the following 3 groups: (1) those that had excisional iridectomy (63); (2) those that had enucleation (72); and (3) those that were observed (22). Patients in the third category were those who were thought to have a probable malignant melanoma based on clinical appearance and behavior but who either refused operation or were not urged to have surgery.

Any pigmented iris lesion showing progressive growth or other evidence of malignant behavior should be excised by means of iridectomy if it seems possible to remove it completely in this manner. A lesion located in the periphery of the iris should be excised early, since any growth would be likely to involve the angle and ciliary body. Enucleation is advisable if the tumor has obviously spread beyond the reach of local excision or there is evidence of residual tumor peripheral to a previously performed iridectomy. The pathological diagnosis of malignant melanoma does not provide grounds for enucleation in the absence of microscopic and/or clinical evidence of remaining tumor. Observation is necessary in any case in which there is not clear-cut evidence of malignant character or behavior, and there are no other indications for surgery.

The over-all mortality in this series, as in other groups reported, was quite low. There were 4 known deaths due to metastatic spread in the 140 cases with follow-up information. Altogether, 60 cases have been followed for 5 years or longer, and 120 cases for 2 years or longer. Of great importance is the fact that no deaths occurred in patients receiving excisional iridectomy as the definitive therapy. It is evident that an iridectomy performed properly at a time when all the tumor can be removed in this manner not only prevents metastatic involvement but avoids the late complications of secondary glaucoma, pain, and blindness which can result from local dissemination. Analysis of the 4 fatal cases shows that enucleation was ultimately performed in each instance. In all these cases microscopic study revealed that the tumor had spread beyond the reach of local excision. In 2 cases excisional biopsies were performed 6 days and 1 week, respectively, prior to subsequent enucleation. In the third case, iridectomies were performed in the course of 2 trephining operations during a 5-month period prior to enucleation, when it was ultimately recognized that the glaucoma present was secondary to a diffuse melanoma of the iris. In the fourth case enucleation was performed without initial iridectomy.

External Ophthalmoplegia as Part of Congenital Myasthenia in Siblings: Myasthenia Gravis in Children: Report of a Family Showing Congenital Myasthenia. F. B. Walsh and W. F. Hoyt. Am. J. Ophth. 47:28-34 (May) 1959 [Chicago].

The authors describe observations on 4 boys with congenital myasthenia and external ophthalmoplegia, who belonged to a family of 6 children in which the parents and 2 daughters were normal. They discuss the various types of myasthenia in children, pointing out that congenital myasthenia is a term used by Levin to describe a form of myasthenia which begins at birth (or before) and is characterized by a mild onset, marked external ophthalmoplegia, partial ptosis, and symmetrical weakness of involved muscle groups. It may be associated with marked weakness of skeletal muscles, especially neck, trunk, and leg muscles. In contrast to the usual form of myasthenia gravis, it is not progressive, does not have remissions, and may improve with time, the response to Prostigmin being dramatic. This disease occurs in siblings without involvement of the parents and is variable in severity. Levin feels that it is not the myasthenia gravis described by Erb and Goldflam, though the basic defect (dysfunction at the myoneural junction) is the same or at least is similar.

The 4 cases presented by the authors closely resembled those described by Levin. Partial ptosis and almost total external ophthalmoplegia were the outstanding findings. One member of this family had severe generalized weakness and fatigability of his skeletal musculature, which was symmetrical and which showed neither remissions nor improvement with time. The response to Prostigmin, though, was dramatic. The use of Prostigmin and electromyography is urged in the differential diagnosis of congenital external ophthalmoplegia.

Arcus Senilis: Its Pathology and Histochemistry. D. G. Cogan and T. Kuwabara. A. M. A. Arch. Ophth. 61:553-560 (April) 1959 [Chicago].

Arcus senilis consists of a peripheral corneal opacity that depends on the presence of proximal blood vessels but yet spares the immediate surroundings of the blood vessels. While present to some extent in all persons past middle age, an arcus is also present occasionally in young persons and is particularly common in persons with familial hypercholesteremia and xanthomatosis. A histological study of 25 eyes obtained through the facilities of the Boston eye bank revealed that arcus senilis is characterized by a hyaline sudanophilia of Descemet's and Bowman's membranes and a granular sudanophilia of the corneal stroma. It is invariably associated with a similar sudanophilia of the anterior sclera. The sudanophilia of Descemet's membrane is noteworthy in that it tends to spare the most peripheral portion of this membrane, and, in its early stages, it involves preferentially the anterior half of this membrane in the form of double laminas. The sparing of the limbus is apparently due to the vascularity of this region. Histochemical and solubility studies of sections from these eyes were performed with the purpose of identifying the fat of arcus senilis. It appeared to be a mixture of cholesterol, phospholipid, and neutral fat. The facts that it may be present in relatively massive amounts, and that it does not depend on any degenerative change in the cornea, suggest that it is derived from the blood and becomes secondarily bound to the tissue. The authors, though, were unable to induce any similar binding in vitro by a comparable mixture of lipids from egg yolk.

THERAPEUTICS

Effect of Drugs on Motion Sickness Produced by Short Exposures to Artificial Waves. E. M. Glaser and R. A. McCance. Lancet 1:853-856 (April 25) 1959 [London].

The authors tested the effectiveness in the prevention or treatment of motion sickness of 4 drugs, hyoscine hydrobromide (in doses of 1 mg.), cyclizine hydrochloride (in doses of 50 mg.), meclizine hydrochloride (in doses of 25 mg.), and perphenazine (in doses of 8 mg.), as well as a lactose placebo; the subjects were 77 soldiers, between the ages of 19 and 25 years, who volunteered for the tests. For an hour after the capsules containing the drugs had been taken, the persons tested were exposed to motion in inflatable tended rubber floats, the position of which in an experimental tank varied from test to test. While exposed to wave motion, the persons were asked to sit up in order to have constant and maximal stimulation of the vestibular apparatus. In the cross-over-double-blind experiment, hyoscine hydrobromide gave significantly better protection against sea sickness than the other treatments. Cyclizine (Marezine) hydrochloride provided somewhat better protection than the undistinguishable lactose placebo. Two commercial preparations of meclizine hydrochloride, Ancolan and Bonamine, as well as perphenazine (Trilafon), were not more effective than the lactose placebo. In single exposures, the lactose placebo appeared to provide significant protection from motion sickness when compared with the effects of no treatment at all. Divergent findings in different experiments could be explained by the possibility that the apparent effects of drugs against motion sickness are sometimes due to psychological reasons, and that the effects of treatment could also be related to the varying susceptibilities of the persons to motion sickness.

Experiences with Isolation-Perfusion Technics in the Treatment of Cancer. O. Creech Jr., E. T. Krementz, R. F. Ryan and others. Ann. Surg. 149: 627-640 (May) 1959 [Philadelphia].

In an attempt to administer effective amounts of cancericidal agents and at the same time reduce the danger of systemic toxic effects, the authors developed the isolation-perfusion techniques for the treatment of malignant lesions. These techniques consist in excluding the tumor-bearing area from the systemic circulation and perfusing it with a chemotherapeutic agent. For tumors on the foot and leg without evidence of inguinal spread, perfusion is accomplished through the common femoral artery and vein. For perfusion of lesions of the hand and forearm, the proximal portions of the brachial artery and vein are used. Exclusion of the lungs is accomplished with the use of 2 extracorporeal circuits. Heart-lung bypass is employed between the venae cavae and the femoral artery, while in the pulmonary circuit blood from the left atrium is routed through a pump oxygenator and returned to the pulmonary artery by gravity. In perfusing lesions within the pelvis, pneumatic tourniquets are placed in the upper portion of both thighs, and the abdominal aorta and inferior vena cava are cannulated near their bifurcation, either directly through an abdominal incision or indirectly by passing catheters through the common femoral artery and vein. Cannulation in the breast is accomplished through the subclavian artery and vein which are reached through the supraclavicular area. For patients whose disease is not regionally confined, a method of perfusing the entire body for treatment of disseminated tumors has been developed also.

During the past 1½ years 73 patients with malignant tumors have been treated with chemotherapeutic agents administered by these techniques. Of the 73 patients, 37 had carcinoma, 18 had sarcoma, and the remaining 18 had melanoma. The chemotherapeutic agents employed were nitrogen mustard, phenylalanine mustard, actinomycin-D, triethylene thiophosphoramide, and 5-fluorouracil, a pyrimidine analog. Of the 73 patients, 56 were treated for palliation of far-advanced malignant lesions, and 17 were perfused in conjunction with extirpation of the primary lesion. Thirteen patients have died. Of the 60 surviving patients, 22 are well, and the lesions appear to be controlled; in 8 the disease is quiescent; and 30 have recurrences. The results obtained suggests that some human cancers can be controlled with chemotherapeutic agents administered in high concentration, but that great variations exist in the response of malignant tumors to these agents. The factors contributing to the response of a malignant tumor after administration of a chemotherapeutic agent by the perfusion technique are not clear. By affording a means for in vivo investigation of tumors in man, the isolation-perfusion techniques may contribute to the understanding of malignant lesions, and ultimately to better therapy.

New Method for Control of Anticoagulation Treatment. P. A. Owren. Tidsskr. norske lægefor. 79:375-379 (April 1) 1959 (In Norwegian) [Oslo].

The new test for control of anticoagulation therapy is about equally sensitive to variations in each of the 4 clotting factors which are reduced during anticoagulation treatment – prothrombin, proconvertin, Stuart Prower factor, and antihemophilic-B factor. The "all-in-one" reagent applied contains an active cephalin-lecithin preparation and a weak thromboplastin reagent, both in optimal concentrations; it also contains stabilized bovine plasma, completely free of the 4 factors to be determined, and calcium in optimal concentration. The dehydrated and vacuum-sealed reagent will keep at least 12 months, and the activity is unchanged after 30 days' storage at 47 C. In solution and ready for use, the activity is constant for at least 12 hours at room temperature. The method has been worked out for capillary blood, citrate venous blood, and citrate plasma, and only 0.10 ml. of blood is needed. The test is quickly and easily performed.

BOOK REVIEWS

Preventive Medicine: Principles of Prevention in the Occurrence and Progression of Disease. Edited by Herman E. Hilleboe, M.D., Commissioner of Health, State of New York, Department of Health, Albany, and Granville W. Larimore, M.D., Deputy Commissioner of Health, State of New York. Cloth. $12. Pp. 731, with 59 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

According to its preface this volume sets forth a new way to look at preventive medicine and is intended for medical students, general practitioners, specialists, and workers in health agencies. It endeavors, through the contributions of 29 experts, to discuss the prevention of disease and to show how a disease, once established, may be managed in its further progress.

Early diagnosis is often impossible because the patient insists on self-medication for the complaint at hand. Then, when it gets beyond relief, he seeks medical advice—often too late. Advances in preventive medicine continue to be publicized in both the medical and the lay press. This is all to the good; for the high hope is that much disease can be prevented if patients, or the public in general, become fairly well acquainted with symptoms which will lead to consultation with doctors of medicine. Unfortunately, this is too often wishful thinking. Further than that, it is sometimes questionable whether we have not overextended ourselves, thus unwittingly establishing a fear complex leading to anxiety and neuroses which are not based on fact. This is an undesirable by-product which is seemingly unavoidable. On the whole, a knowledge of prevention of both accidents and disease is highly desirable; it is a question of the greatest good for the greatest number.

Much of the material in this book has been set forth in magazines, pamphlets, and public lectures. Publicity concerning the newer remedies is so well distributed that a patient may confound his physician with news of some remedy that was too highly praised in the morning paper. Neither doctor nor patient can know everything about everything.

In general the authorities who have contributed special articles to this volume write from experience, but it might have been just as well to limit the discussion to prevention and to have omitted part 2 which deals with prevention of progression. Another and different volume might well be written on this phase. For the physician who wishes to learn how to halt a chronic or well-established condition, there is still much to be discovered. In part 2 the editors of this volume have limited themselves to a discussion of periodic health inventories, cancer detection and screening, and have done the same for pulmonary tuberculosis, heart disease, diabetes mellitus, and hearing and visual defects. In section C there is a follow-up of such screening and diagnostic examinations, and other sections deal with rehabilitation, alcoholism, and narcotic addiction. Part 3 is devoted to health education for the public and postgraduate studies for the physician. There are chapters on social work, public health nursing, the role of the hospital, epidemiologic methods and inference, and a final chapter on official and voluntary health agencies. This book attempts to cover too much ground and in too sketchy a manner. For the most part it is written in a fluent style, without disturbing and difficult technicalities. This makes for easy reading by nonmedical persons as well as the medical profession.

Staphylococcus Pyogenes and Its Relation to Disease. By Stephen D. Elek, M.D., D.Sc., Ph.D., Professor of Bacteriology in University of London, London. Cloth. $15. Pp. 767, with 45 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

Professor Elek's new book is written for scholars in the field of bacteriology. It is not a compendium of information of general interest to clinicians. On the other hand, it should be read with great care by any clinician to whom the responsibility for staphylococcic infections has been given. The most unusual and complete bibliography, which comprises some 188 pages of the volume, is well worth the cost of the book. The sections entitled Historical Survey and Problems of Taxonomy are written as only an expert could write them. In the field of metabolism of staphylococci the volume leaves something to be desired if it is viewed by a biochemist or microbiologist with particular leanings toward chemistry. A clear elucidation of the status of knowledge concerning phage, lytic phenomena, and coagulase reactions is given. The peculiar relationships between virulence and the simple presence of organisms which could be virulent in the environment of man are stressed and described. Many features of this aspect of staphylococci and their behavior remain to be clearly described. Chapter 14, which deals with antibiotics, gives a superb account of the historical aspects of the development of antibiotics, the mode of their action, the situation with regard to antibiotic-resistant strains of staphylococci, and specific considerations of other antibiotic substances. Such a book should be a welcome addition to a good medical library at any time. Coming at a time when there is an international problem of antibiotic-resistant staphylococci that have apparently increasing virulence for man, the book stands alone as a guide to this entire subject.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

DETERMINATION OF PARENTAGE

To the Editor:—*When a child's mother is missing, are there tests, blood or other, which could prove or disprove parentage of a man suspected of being the father?*

M. A. Shillington, M.D., Brainerd, Minn.

Answer.—In disputed paternity proceedings, blood grouping determinations offer a reliable scientific means of solving the question in many cases. Paternity can never be proved by means of blood tests. However, nonpaternity can be proved in a considerable proportion of the cases by an accurate analysis and comparison of the four main groups and the various subgroups of the child, mother, and alleged father. Even in the absence of the mother, in some cases it is possible to prove nonpaternity. For example, a man belonging to group AB cannot be the father of a child with group O and a man with group O blood cannot be the parent of a child with group AB. Also, a man with type M cannot be the father of a child with type N, nor can a man with type N have a child with type M. Such determination should be conducted only by a serologic laboratory that is constantly doing this type of work and in which there are adequate facilities for checking and rechecking the serums used and the results obtained.

AMEBIC DYSENTERY PROPHYLAXIS

To the Editor:—*If one goes to an area where the incidence of amebic dysentery is high, what is the effectiveness of using an amebicide, such as glycobiarsol, prophylactically? Does such medication prevent clinical infection or does it merely suppress symptoms? What is the adult and child's dosage schedule, and over how long a period can it be used?*

Fordyce L. Howe, M.D., Fort Wayne, Ind.

Answer.—Chemoprophylactic investigations by Beaver (*Am. J. Trop. Med.* 5:1015, 1956) showed that the daily administration of 250 mg. of glycobiarsol not only protected against infection with Entamoeba histolytica but also terminated infection in infected controls. Sanchez Vegas (J. A. M. A. 151:1059-1065 [Marclr 28] 1953) administered glycobiarsol to 87 persons suffering from intestinal amebiasis. He used larger doses than are currently recommended (1 Gm. three times daily, after meals, for 35 days). Some of his patients received as much as 200 Gm. of glycobiarsol during the entire course of treatment. Of 87 patients given these large doses, 2 complained of headache and transitory urticaria, 16 of pruritus ani, 26 of flatulence, and 28 of indigestion. Glycobiarsol can be used effectively in the prophylaxis and treatment of amebiasis, and it can be used over a long period provided the person is not allergic to arsenicals or bismuth. The recommended prophylactic dose is one tablet (250 mg.) once daily for children over 10 years of age and adults and one-half tablet once daily for children under 10.

The inquirer made no mention of the country to be visited. If malaria is also endemic in the area, glycobiarsol-chloroquine phosphate combination tablets would be the agent of choice, for they would not only protect against malaria and intestinal amebiasis (Berberian and others, *J. A. M. A.* 148:700-704 [March 1] 1952) but also prevent systemic dissemination and extraintestinal localization of amebas. Each tablet contains 250 mg. of glycobiarsol and 75 mg. of chloroquine. The prophylactic dose would be one tablet per diem for adults and one-half tablet for children.

UNILATERAL KIDNEY CYST

To the Editor:—*Should asymptomatic unilateral cyst of kidney be treated surgically? If so, should nephrectomy, heminephrectomy, or cyst excision be done?* *W. S. Levy, M.D., Woonsocket, R. I.*

Answer.—In general, asymptomatic unilateral cyst of the kidney should be treated surgically. The reason for this is the difficulty in positively excluding a malignancy of the kidney in the differential diagnosis. Aortography has been suggested as a means of making this differential diagnosis, but this it not always satisfactory. Needle biopsies have also been done on patients of advanced age in an effort to settle the diagnosis. If the fluid obtained is clear and straw colored, there is some assurance that a cyst is present. However, in most instances, surgical exploration in the flank area, with exposure of the kidney, can be carried out with minimal risk and more accurate evaluation obtained. If the cyst is found to be very large and has compressed or destroyed a fair portion of the kidney, nephrectomy is the procedure of choice. If, however, an appreciable amount of functioning renal tissue remains, incision of the cyst with close inspection of the point of attachment to the renal parenchyma is indica Many times in the base of the cyst there is a fluence of blood vessels with proliferative t

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

changes, sometimes suggesting an underlying malignancy. If there is any question of this, nephrectomy is indicated. However, malignancy within a renal cyst is uncommon. If the cyst seems to be definitely benign, its excision close to the margin of the renal parenchyma, with suture of the cyst edge to the adjacent renal parenchyma with a superficial mattress suture, is indicated. If there is any question of the edges of the cyst approaching one another it is well to pack the cavity with iodoform gauze for a period of time. If it seems advisable to remove the base of the cyst from the renal parenchyma, it is better to carry out partial nephrectomy, keeping the incision line at least a centimeter away from the base of the cyst. This will avoid extensive bleeding in many instances.

SUPERFICIAL PUNCTATE KERATITIS

To the Editor:—*What is considered the most effective treatment for superficial punctate keratitis? This case has persisted for six months and has shown no improvement with chloramphenicol eye drops and sulfacetamide sodium. Does the latter retard healing of corneal epithelium? Is there any danger from an infra-red heat lamp used for five minutes several times each day over a long period of time? Would Microtherm therapy help, or would it be contraindicated? Several cultures and smears are negative.*

M.D., North Carolina.

Answer.—Superficial punctate keratitis is considered to be due to a virus infection. At present, there is no known treatment for this condition that can be used with assurance of success. Chlortetracycline and chloramphenicol as eye drops are considered the most effective local antibiotics. Cauterization of the corneal epithelium with weak iodine solution or ether is effective in many cases. More drastic treatment would be to denude the corneal epithelium with forceps or by scraping, and then cauterize with iodine or ether. The eye is then bandaged. Potassium iodide in a 2% solution as eye drops has been used with benefit. The oral use of sodium iodide solution, giving 1 grain (65 mg.) per 10 lb. of body weight three times daily for 10 to 14 days, is helpful if started early. The corticosteriod drugs given locally or systemically are contraindicated. Cold compresses to the eye may afford relief. Sulfacetamide sodium as an ointment may retard corneal epithelial healing, as many ointment bases will do. In drop form, the drug is not known to retard healing. Use of infra-red or any form of heat is contraindicated because it is believed that viruses thrive on mild heat. Microtherm therapy is contraindicated on the same premise. It is not uncommon to overtreat a case such as this, and if all else fails treatment might be stopped entirely except for the use of an eye wash of isotonic sodium chloride solution.

EFFECTS OF "HOT ROAD OIL"

To the Editor:—*A state insurance fund has asked whether hepatitis in an employee may have been due to breathing smoke from "hot road oil" used in patching asphalt roads. This mixture consists of asphalt, tar, and possibly some other ingredients which are heated to high temperatures with butane or kerosene. Since this material is used widely throughout the United States and no report has been seen of a resulting hepatitis, the etiological implications are questionable. However, so that no injustice is done to the patient, please give further information. There have been no hematological or neurological changes, and the patient has fully recovered. The inhalation occurred over a period of six months or more.*

R. P. Howard, M.D., Pocatello, Idaho.

Answer.—As the inquirer states, thousands of road workers using asphalt follow daily practices that are much the same over the entire United States. The chemicals are nearly the same, and likewise the fuels. Moreover, this type of work has been going on for about 50 years. If hepatitis was an expectable result of exposure it would have attracted medica attention long ago. Such is not the case. What ma be indicated here is exploration of the method o skin clearing after work. After the workman is lef to his own devices he may use almost any chemica detergent. If this workman resorted to use of a sol vent such as carbon tetrachloride, even in smal amounts and for brief periods, the occurrence o chemical hepatitis is plausible.

PREGNANCY AND KERATOCONUS

To the Editor:—*A woman with keratoconus has had three successful pregnancies. During each pregnancy, there was deterioration of visual acuity which was brought up to 20/30 or better by a change in glasses. She is pregnant again, and the question has been raised whether therapeutic abortion and sterilization is justified.*

Raymond S. Goux, M.D., Detroit.

Answer.—Keratoconus, or conical cornea, is a noninflammatory condition of the cornea which may be either rapidly or slowly progressive. It is more common in females and in some cases may be hereditary, though this is by no means common. The consensus is that there is some relationship between the development of conical cornea and the endocrine system. Therefore, it is natural to expect the condition to become worse after each pregnancy. However, as most cases of conical cornea progress over a period of years, it is a matter for individual decision as to whether pregnancy should be interrupted. If the change has been of 3 or 4 D. each time, one would feel justified in advising therapeutic abortion. In other words, if one can be sure that pregnancy definitely aggravates the condition to a marked degree, abortion and sterilization should be performed. Corneal transplantation will arrest keratoconus to a marked degree and restore the patient's vision to nearly normal provided operation is performed when the condition is not too far advanced.

ELBOW DISLOCATION IN A CHILD

To the Editor:—*Children under 2 or 3 years of age who have dislocated an elbow have often been seen. Treatment has included reduction as an office procedure, without use of x-rays. Is this a risk, from the viewpoint of malpractice? The whole procedure has seemed so simple that additional treatment appears unnecessary.*

M.D., Massachusetts.

Answer.—Dislocation of the elbow in a child of 2 or 3 years is quite unusual. On the other hand, the so-called luxation of the head of the radius in relation to the annular ligament is quite common. The area is maintained in pronation, and any attempt at motion is quite painful. This luxation can be readily reduced by supinating the hand. It would seem likely that this is what is meant in the question. True dislocation of the elbow is of such importance that x-rays ought to be taken. Dislocation may be associated with other injury, such as displacement of the medial condylar epiphysis, which x-ray would show. If it is difficult to obtain an x-ray immediately and the child shows undoubted symptoms of dislocation of the elbow, general traction followed by bringing forward the distal unit with flexion may be carried out to see if reduction may be accomplished. One must depend greatly on traction. Manipulation must be done most judiciously. X-rays should be taken afterward to be sure the epiphyses are in proper position.

ALUMINUM INHALATION THERAPY

To the Editor:—*What is the present medical opinion regarding efficacy of aluminum inhalation therapy for prevention and treatment of silicosis in the sanitary pottery industry?*

D. C. Simmons, M.D., Kilgore, Texas.

Answer.—Present opinion on the therapeutic and prophylactic use of aluminum inhalations with silicosis still is somewhat divided. A statement which seems to represent the thinking of most authorities on the subject can be found in the book by Patty entitled "Industrial Hygiene and Toxicology" (New York, Interscience Publishers, Inc., 1958, vol. 1, pp. 394-397). The statement is made that all possible methods of preventing silica dust dissemination in the working atmosphere must be used before considering aluminum dusting. It is recognized that satisfactory engineering control of dust in the pottery industry is difficult to achieve, especially when the content of crystalline-free silica in the clay is high. If silicosis still develops among workers in spite of the best kind of dust control available, then the use of aluminum inhalation may be justifiable on a preventive basis only. Its use in treatment of an already-established case of silicosis cannot be justified, however, except on a purely psychological basis.

CARDIAC PACEMAKER

To the Editor:—*A cardiac pacemaker and a cardioscope have been acquired in the local hospital. There has been considerable controversy as to proper use in cardiac conditions other than the asystole encountered during anesthesia. Will attaching the cardiac pacemaker to a normal person for demonstration purposes entail any danger to the subject? Is the cardiac pacemaker of any value in treating extrasystoles, paroxysmal tachycardia, auricular flutter, auricular fibrillation, or any nodal or idioventricular arrhythmia?*

Robert L. Salb, M.D., Crossett, Ark.

Answer.—It is probably not advisable to attach the cardiac pacemaker to a normal person. The cardiac pacemaker might interrupt the subject's normal cardiac rhythm, and this could be dangerous. Thus far, it has not been proved that the cardiac pacemaker is of any value in the treatment of extrasystoles, paroxysmal tachycardia, auricular flutter, auricular fibrillation, or nodal or supraventricular arrhythmia.

THROMBOEMBOLIC EPISODES

To the Editor:—*Is there any evidence that administration of diuretics, as for congestive heart failure, predisposes to or tends to precipitate thromboembolic episodes, especially in cerebral vessels?* *Collin Baker, M.D., Tampa, Fla.*

Answer.—It has not been shown that administration of diuretics to patients with congestive heart failure in any way predisposes or causes thromboembolic episodes. It was once thought by a few workers that administration of digitalis to patients with congestive heart failure predisposed to such episodes, but this too has been definitely proved untrue.

LOSS OF SKIN PIGMENT

To the Editor:—*Please give information concerning development of vitiligo, secondary to a rash, in a person who processes the plastic Bakelite.*

Robert C. Puestow, M.D., Manitowoc, Wis.

Answer.—Loss of pigment after an inflammation such as a dermatitis is properly called a leukoderma. It is usually temporary. A condition resembling vitiligo may be observed after exposure to monobenzylether of hydroquinone. This antioxidant found in rubber. The mechanism is an actual inhibition of melanin formation. It has also been found that hydroquinone and p-hydroxypropiophenone are effective inhibitors of mammalian melanin formation. So far as is known, these chemicals are not encountered in the manufacture of Bakelite.

WAX AS CARCINOGENIC FACTOR

To the Editor:—*The question has been asked whether the wax coating on the inside of milk cartons may be carcinogenic, since it has been reported to have produced carcinoma in mice. Might it be a contributing factor in carcinoma of the bladder or elsewhere?*

M.D., West Virginia.

Answer.—*Development of papillomas in the bladders* of rats after implantation of paraffin pellets has been reported by Bonser. In another unreported but verified study, implantation of paraffin pellets in the bladders of mice resulted in papillomas and cancers. While the majority of commercial waxes are apparently free of significant amounts of known carcinogenic impurities, several have been demonstrated to contain dibenzanthracene. This may be released into milk. The American Petroleum Institute, at the instigation of the Milk Industry Foundation and other interested groups, has been conducting research on this problem (*News Letter* of the Milk Industry Foundation, March 30, 1959).

ATOPIC DERMATITIS AND CLIMATE

To the Editor:—*In* The Journal, *Jan. 17, 1959, page 306, in Questions and Answers, a question was raised about atopic dermatitis and climate. The consultant's discussion of the climate factor was quite good. In his opening remarks, he mentioned the possibility of the development of other manifestations of atopy and in his concluding remarks, the financial burden and family disarrangement involved. It seems to me that he could have mentioned that a complete allergic survey and good allergic management would be a more rational approach in such a case.*

Edward Pickert, M.D.
679 Irvington Ave.
Newark 6, N. J.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The question originally asked was specifically in respect to the relief of atopic dermatitis which might be achieved by climatologic therapy. In a short reply, it was not possible to present all the methods of management which have varying effects in this difficult clinical syndrome. Allergic management is one of these, though it, like all other methods of treatment, fails in many cases. It is the opinion of this consultant that chief emphasis in respect to an allergic component should be placed on a carefully taken history and observation of the patient, in respect to exacerbations which might be attributable to clinical exposure to various ingestant and inhalant allergens. Unfortunately, allergic management based primarily on the results of scratch and intradermal tests and on attempts at hyposensitization and procedures is infrequently effective and sometimes harmful. It is characteristic of atopic dermatitis that there are multiple reactions to a wide variety of scratch tests and that there is often no relation of the specific positive tests to the dermatitis. There is considerable controversy on this matter, some of it quite vehement, but it can be confidently stated that the conditions of too many patients with atopic dermatitis are managed routinely on this basis with little likelihood of benefit. If scratch and intradermal tests are carried out, the relation of specific positive reactions to the dermatitis should be confirmed or disproved clinically if at all possible. It is unwise to restrict the patient's environmental contacts, or his diet, or to undertake interminable courses of "hyposensitizing" injections unless some good is likely to result therefrom.*

WEIGHT GAIN AFTER CESSATION OF SMOKING

To the Editor:—*The answer to Dr. Trapnell's question on weight gain after stopping smoking (J. A. M. A.* 169:*1269 [March 14] 1959) implies that ingested calories are absorbed from the intestine at the same rate whether one smokes or not. Could you supply confirmatory data?*

Armistead D. Williams, M.D.
The Chesapeake and Ohio Hospital
Clifton Forge, Va.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*A survey of the current literature and contemporary textbooks on pharmacology and physiology reveals no reference to any alteration of absorption effected by smoking and/or nicotine.*

G.C.P.J.—541-10,000-08.